REVIEW OF THE DEPARTMENT OF ENERGY'S HEALTH AND MORTALITY STUDY

HEARING

BEFORE THE

SUBCOMMITTEE ON
INVESTIGATIONS AND OVERSIGHT

OF THE

COMMITTEE ON
SCIENCE AND TECHNOLOGY
U.S. HOUSE OF REPRESENTATIVES

NINETY-SEVENTH CONGRESS

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REVIEW OF THE DEPARTMENT OF ENERGY'S HEALTH AND MORTALITY STUDY

WEDNESDAY, MAY 19, 1982

House of Representatives,
Committee on Science and Technology,
Subcommittee on Investigations and Oversight,
Washington, D.C.

The subcommittee met, pursuant to call, at 1:50 p.m., in room 2325, Rayburn House Office Building, Hon. Albert Gore, Jr. (chairman of the subcommittee) presiding.

Mr. Gore. The subcommittee will come to order.

I would like to apologize for the delay in opening. The Science and Technology Committee has the National Science Foundation bill on the floor, and there have been votes, and that is the reason for the delay. Some of you have an interest in seeing that bill passed.

I would like to welcome all of our guests and distinguished witnesses.

Today the Subcommittee on Investigations and Oversight will be examining DOE's health and mortality study being conducted by the Oak Ridge Associated Universities. This study is one of 16 studies on low levels of ionizing radiation being conducted by DOE. This study was selected because it has the largest study population by far and its findings could have a major impact on the nuclear industry.

The subcommittee has invited panels of experts to discuss the three major areas of inquiry for today's hearing.

The first panel will discuss the design and objectives of the health and mortality study. There are inherent limitations in any epidemiologic study, such as inadequate records and dosimetry data, healthy-worker syndrome, exposure to chemical agents or other confounding factors, and insufficient study population. We intend to examine how this study is dealing with such factors and how well the objectives are being met.

The second panel will discuss the value of this study. The number of workers being studied that have been exposed to 1 to 5 rems annually—approximately 100,000 man-years—and to more than 5 rems annually—approximately 2,000 man-years—may represent populations that are too small to permit derivation of statistically meaningful data.

If this is the case—and I don't want to prejudge that conclusion—what scientifically meaningful data can be expected? In addition, these experts will be asked to review some of the recommendations of various committees that have reviewed DOE's studies on low levels of ionizing radiation.

The third panel will discuss what our future Federal research efforts should be. Given the importance of safeguarding the health of nuclear workers and the inherent limitations of epidemiologic studies of low levels of ionizing radiation, this discussion is particularly pertinent.

We need to consider the development of biological and biochemical markers related to both dose received and disease contracted, studies of end points other than mortality, and the establishment of prospective rather than retrospective studies. Lastly, we will hear from the Environmental Policy Center.

This hearing should provide information which we anticipate will be helpful in assisting Congress to review radiation health and safety programs, and research presently being conducted. I would like to invite our first panel of witnesses to come to the table: Dr. J. W. Thiessen, Acting Deputy Associate Director of the Office of Health and Environmental Research with the Office of Energy Research in the Department of Energy; Dr. C. C. Lushbaugh, director of the medical and health sciences division, Oak Ridge Associated Universities at Oak Ridge, Tenn.; and Dr. Carl Shy, Department of Epidemiology, School of Public Health, University of North Carolina.

If the three of you would come to the witness table, we would be delighted to hear from you.

If you would raise your right hand.

[Witnesses sworn]

Mr. GORE. As an investigative subcommittee, we follow that practice. Mr. Walker was just successful in passing his amendment. That is bad news for those of you who don't know the details.

Without objection, the prepared text of all three witnesses will be put into the record in full, and we would like to proceed with the presentation now, starting with you, Dr. Thiessen.

STATEMENT OF DR. J. W. THIESSEN, M.D., ACTING DEPUTY ASSOCIATE DIRECTOR, OFFICE OF HEALTH AND ENVIRONMENTAL RESEARCH, OFFICE OF ENERGY RESEARCH, DEPARTMENT OF ENERGY; CLARENCE LUSHBAUGH, PH. D., M.D., MEDICAL AND HEALTH SCIENCES DIVISION, OAK RIDGE ASSOCIATED UNIVERSITIES, OAK RIDGE, TENN.; AND CARL SHY, M.D., DR.P.H., DEPARTMENT OF EPIDEMIOLOGY, SCHOOL OF PUBLIC HEALTH, UNIVERSITY OF NORTH CAROLINA

Dr. THIESSEN. Mr. Chairman, with your permission I would like to summarize my written statement and clarify some of the issues raised by the subcommittee.

In the first place, we would like to thank you for the opportunity to discuss the Department of Energy's health and mortality study which we believe is one of our most important efforts in the framework of the entire epidemiologic program carried out by the Office of Health and Environmental Research.

The total expenditure will amount to approximately $17 million in 1982, for the entire epidemiologic investigation area. About 55 percent of that amount is spent on the investigation of the Radiation Effects Research Foundation in Japan; 15 percent on the radium dial painters; and roughly 20 percent, or $3.3 million, for the health and mortality study. So, it is a major part of our epidemiologic research efforts.

Although conceptually one study, the DOE health and mortality study is carried out in a number of locations; as far as the Hanford population is concerned, part of the study is carried out by the Hanford Environmental Foundation and Battelle Pacific Northwest Laboratories.

The study on the plutonium work is carried out at Los Alamos National Laboratory. Oak Ridge Associated University takes care of all other populations back to Manhattan Engineer District workers, and is responsible for the interface with the Social Security Administration for obtaining death certificates and for maintaining certain computer bases data, et cetera.

In this oral statement I would like to elaborate on two issues raised by the subcommittee and others.

The first one is, why do the health and mortality study at all? In other words, what are the objectives from our point of view? The second issue I would like to discuss with you now is the matter of peer review.

As far as the objectives are concerned, the primary reason for the study is to discharge our responsibility as an employer for the well-being and protection against health hazards of our employees and the employees of our contractors.

Consequently, the evaluation of occupational health hazards, in our view, is based primarily on that consideration. It is not particularly directed toward—I would like to make that specifically clear—determining health effects from low-level ionizing radiation. We do analyze, of course, health and mortality statistics, but primarily to determine whether health effects are more serious than those projected on the basis of extrapolation from high dose data.

Consequently, the most we can hope to get out of it is the demonstration that low-level radiation effects are not more serious than generally assumed. But that point is very important and well worth more remembering.

With regard to peer review, we consider that such a process is of the utmost importance. It certainly is as related to things such as credibility and quality of the entire effort, the direction of and the priorities within the study. We are and have been taking steps to strengthen that process.

Now I would like to mention a number of forms of peer review that I think ought to be recognized, because very often it is thought that peer review is a matter of advisory panels and that kind of thing. I don't think that is true. I think things such as interactions among colleagues, attendance at workshops, publications in refereed journals, and presentation of papers at scientific meetings are all forms of peer review, or are very much related to peer review.

Certainly program advisory panels are of importance. The one at ORAU, for example, meets once a year. Dr. Hutchison, the chairman of that panel, is here and will testify later.

That panel certainly has an influence with respect to the peer review of what is happening in the framework of the health and mortality study, but it is only one factor, and I would like to stress that. There are other factors. Many laboratories have visiting committees that look at the entire program and certainly look at the epidemiologic efforts going on. Probably of more importance are the research planning group meetings between the University of North Carolina and ORAU, which take place once a month.

These are all forms of peer review that I think ought to be recognized as such, because I believe that peer review is an integral part of the scientific process. It is not a system that the Government imposes upon its investigators.

We expect all of our scientific investigators to adhere to and comply with the general rules to which any scientific project is subject. Consequently, we do expect our investigators to publish in the referred literature, and we still believe that this and all of the other factors I have mentioned represent quite extensive peer review and quite extensive assurance that projects are proceeding in accordance with the general rules as to quality common in the scientific community.

On the Government level, of course, there are a number of actions that do relate to peer review because they clearly involve an exchange of scientific information. For example, proposals are extensively reviewed, usually by mail review. Our own staff is heavily involved with that.

We have a research committee in the Office of Health and Environmental Research that reviews every proposal. There are site visits from headquarters staff, usually accompanied by experts in the particular field that we are investigating.

The National Academy of Sciences has recommended that OHER should have an epidemiology advisory committee. Let me mention we had an advisory committee for biology and medicine. It was established in 1947 and was abolished in 1974 when AEC became ERDA.

In 1976, an environmental advisory committee was established. However, it was not until 1979 that the first meeting took place.

At that point in time, the Office of Health and Environmental Research was moved into the Office of Energy Research and basically we became subject to—although formally we already were—reviewed by the Energy Research Advisory Board.

What I am saying is that we do have a system of advisory committees. We do not have an advisory committee with respect to the epidemiology program, but as I hope I have made clear, I don't think that is the crux of the matter.

The crux of the matter is that we expect any scientific enterprise that we are supporting to proceed according to general rules that apply to any scientific research. Then, of course, there is the interaction with the staff, especially the Human Health Assessment Division. Dr. Joseph Blair, Director of that Division is here today, and Dr. Robert Goldstmith, sitting behind me is the staff epidemiologist. We consider this interaction an extremely important part of the peer review.

In summary, we do agree that peer review is extremely important and responsible, in part, for the credibility and quality of the entire effort. However, as I explained before, I do believe that peer review is an integral part of the scientific process and not necessarily just an independent sort of system or oversight to be established by the Government.

Mr. Chairman, as many expert witnesses will explain, and as you have indicated in your opening statement, retrospective studies have inherent problems with respect to the interpretation of results.

There is no question that we have to somehow get into a prospective study design where we develop a data base for continuous epidemiologic evaluation. Efforts are underway to allow this. At the moment, within our own office and with the Office of Operational Safety at the Department of Energy, we are developing a health information system that will collect all of those end points, some of which you have mentioned yourself, that we will be able to evaluate once the system is in place.

This concludes my oral remarks.

[The prepared statement of Dr. Thiessen follows:]

Testimony Before House Committee on Science & Technology
Subcommittee on Investigations & Oversight

J. W. Thiessen, M.D.
Acting Deputy Associate Director
Office of Health and Environmental Research
Office of Energy Research
Department of Energy
May 19, 1982

On behalf of the Department of Energy (DOE), I appreciate the opportunity to discuss our epidemiologic research program, and in particular, the DOE Health and Mortality Study. As shown in the attached table, the major DOE epidemiologic studies involve a total of more than one million persons, principally in occupational settings; and in terms of budget and study population size, emphasize populations with exposure to ionizing radiation. These groups range from Japanese atomic bomb survivors with high dose, acute exposures to nuclear shipyard workers and DOE/DOE contractor employees with low dose, chronic exposures. As a whole, the program in radiation epidemiology represents the largest Federal government effort to examine the human health effects associated with exposure to ionizing radiation in the workplace and general environment. The Health and Mortality Study itself involves over 600,000 workers with both internal and external radiation exposures. In addition, these workers may have been exposed to chemicals and other occupational hazards with effects similar to those from radiation exposure.

The Health and Mortality Study contains three principal segments which focus on specific worker populations. Past and present employees of the Hanford facility in Richland, Washington, are studied jointly by the Hanford

Environmental Health Foundation, which is responsible for data collection, and the Battelle-Pacific Northwest Laboratories, which performs the data analysis. The Los Alamos National Laboratory (LANL) conducts studies of workers exposed to plutonium at several DOE facilities. These include the only long-term medical observations of persons with high plutonium body burdens. The Oak Ridge Associated Universities (ORAU) is responsible for studying all other DOE and DOE contractor employees and for administering the DOE/Social Security Administration (SSA) interagency agreement for vital status searches needed by all study components. ORAU also provides death certificate retrieval, and International Classification of Disease (ICD) coding for the ORAU and Hanford segments.

The Health and Mortality Study has produced important findings on the health effects associated with occupational exposure to low-level ionizing radiation and other hazards found in the workplace. Among these results are the following:

- o After 32 years of medical follow-up, no evidence to date to suggest that adverse health effects have resulted from exposure to internally deposited plutonium among twenty-six male Manhattan Engineer District workers, including eleven with depositions greater than the current maximum permissible body burden.
- o Estimates of mortality risk from lung cancer due to plutonium exposure, significantly higher than those generally accepted by the scientific community, are not supported by actual data on humans.
- o Preliminary evaluation of mortality data on workers at the Rocky Flats Plant indicates an apparent excess number of deaths due to intracranial tumors.

- Workers exposed to phosgene at a uranium processing plant have excess mortality from respiratory diseases.
- Excess mortality from emphysema was found in a study of welders at one nuclear facility.
- No evidence for increased mortality from cancers of bone, blood-forming organs or lymphatic tissue was found in a study of workers at early uranium processing plants.

These are just a few examples of direct results from the Health and Mortality Study, which have been published in the open scientific literature after appropriate peer review by experts in the field. Indirect results of the study include recognized advances in biostatistical methodology and occupational health surveillance data management.

The purpose of the Health and Mortality Study is twofold: Firstly, in conjunction with other DOE studies and with the historical precedence afforded by DOE's predecessor agencies, the Health and Mortality Study attempts to assess the impact of radiation exposure on human health. As such, the study involves one of the largest healthy populations chronically exposed to low-level ionizing radiation, and represents our best chance for a better understanding, based on direct observation, of health effects resulting from such exposures. Secondly, the Health and Mortality Study helps fulfill DOE's responsibility to protect the health and safety of its employees and employees of its contractors by evaluating the morbidity and mortality experience of these workers.

The Health and Mortality Study has evolved into its present form by a combination of need for scientific information, concern for the protection of the health of DOE workers and response to public and Congressional concerns.

In addition, we have considered comments made by the National Academy of Sciences (NAS) with respect to establishment of a uniform peer review process and an advisory council to oversee the research program for the entire Office of Health and Environmental Research (OHER). Except for a short period of time, OHER and its predecessors have had an advisory committee: from 1947 until 1974, the Advisory Committee for Biology and Medicine (ACBM) and from 1977-1981, the Environmental Advisory Committee. However, committees such as these, with their "broad-brush" approach do not provide the intensive, project-by-project technical review which is necessary for quality project management. The structure and mission orientation of DOE require a different approach which marries agency objectives with scientific quality. Our system of ad-hoc periodic review at both universities and national laboratories by on-site visits of experts in the field is more effective.

Each of the the Health and Mortality Study components has an advisory panel which reviews the progress and merits of the study, as recommended by NAS. Although OHER usually has a representative at advisory committee meetings, we are initiating formal peer review site visits to all of our epidemiology contractors for an independent assessment of the entire program. This type of comprehensive project-by-project review is common throughout OHER, and is overdue in our epidemiology program.

Questions have been raised regarding our use of a DOE laboratory instead of a university for the conduct of the Health and Mortality Study. When the main portion of the study was transferred to ORAU, however, the laboratory (which actually is a consortium of over 50 universities) was requested to identify epidemiologic and biostatistical expertise at one or more of its member universities to work with ORAU. The University of North Carolina (UNC), recognized in the field for its excellence in epidemiology and biostatistics and an acknowledged leader in occupational health studies, now shares responsibility for the Health and Mortality Study with ORAU. The merging of state-of-the-art technical skills found at universities such as UNC, with the stability, the diversity of professional and technical expertise and the ability for quick response found at ORAU, provides, in our view, the best of both worlds.

We have redoubled our efforts to improve communication and achieve better coordination among the Health and Mortality Study segments and other studies of the health effects of ionizing radiation supported by DOE and other Federal agencies. Under the direction of our staff epidemiologist, we recently sponsored a workshop which brought together the principals and staffs of all of our radiation epidemiology studies as well as representatives from several other Federal agencies. In addition to responding to the NAS recommendation for better coordination among projects in general, and regarding the Death Certificate Retrieval Office in particular, this workshop explored the complexities of another recommendation — implementation of a uniform exposure record and data collection system. Moreover, the workshop participants began the long and difficult task of determining the feasibility, advantages, disadvantages, and advisability of pooling populations from various facilities in order to achieve higher statistical power. Work is now well under way, however, towards developing a uniform data collection system for use in all segments of the study.

The difficult nature of epidemiologic research on low-level ionizing radiation has been widely recognized. Yet, we need to conduct this type of research to be responsive to the concerns of the public and protective of the health of our workers. This type of research is expensive, complex and likely not to be definitive. However, we agree with the view expressed in the NAS Report that "Nevertheless, the pursuit of such research, even at considerable cost, is justified by the possibility that the effects of low doses of ionizing radiation are greater than currently estimated."

We believe the program to be of high quality and expect it, in fact, to improve as we implement such innovations as use of the National Death Index, development of an agency-wide Health Information System, and, possibly, establishment of a national radiation worker registry. Thus, we will be able to escape our dependence on existing exposure records and on mortality endpoints, as we move into a prospective study design which will allow us to better examine the occurrence of a variety of health effects.

DOE EPIDEMIOLOGIC STUDIES

STUDY POPULATION	TYPE OF EXPOSURE	NUMBER OF SUBJECTS
ATOMIC BOMB SURVIVORS (RERF)	HIGH DOSE, ACUTE EXTERNAL	170,000
DOE/DOE CONTRACTOR WORKERS	LOW DOSE, CHRONIC EXTERNAL	600,000
NUCLEAR SHIPYARD WORKERS	LOW DOSE, CHRONIC EXTERNAL	250,000
PLUTONIUM WORKERS	CHRONIC, INTERNAL	15,000
RADIUM DIAL PAINTERS	CHRONIC, INTERNAL	10,000
CYCLOTRON WORKERS	MAGNETIC FIELDS	750
U.S. OIL SHALE WORKERS	SHALE OIL AND RELATED PRODUCTS	87+
SCOTTISH OIL SHALE WORKERS	SHALE OIL AND RELATED PRODUCTS	10,000
U.S. GENERAL POPULATION	CARBON MONOXIDE	9,000

Mr. GORE. Thank you very much.

Dr. Lushbaugh, we have another vote on the floor. Maybe instead of interrupting your statement in the middle, we will break at this time. This will be a much shorter break than the last one because we have only one vote instead of two.

This is the Walker amendment, and quite an important one. We will recess very briefly.

[Recess.]

Mr. GORE. The subcommittee will come back to order.

Dr. Lushbaugh, welcome back to the subcommittee. We appreciate you being here. Please proceed as you see fit. Without objection, all of the text will be put in the record and you may present any or all of it.

Dr. LUSHBAUGH. I have asked Mr. Robie to assist me in showing my viewgraphs out of my written testimony. So, I will read an oral statement, which is a summary of my extended statement.

Mr. Chairman, I appreciate this opportunity to provide information concerning the ongoing Department of Energy's health and mortality study being conducted in part by Oak Ridge Associated Universities under my direction.

I am accompanied today by Dr. Carl Shy, professor of epidemiology of the school of public health, University of North Carolina, who is coprincipal investigator with me on these studies.

Dr. Shy leads a subgroup of occupational epidemiologists and staff persons located at the Chapel Hill, N.C., campus. Dr. Shy will describe to you the scientific epidemiologic problems our combined groups are addressing, while I describe the more pragmatic ones.

We have put together a well-trained group of scientists and technicians who are overcoming the problem of studying the extraordinarily large data base of Oak Ridge, which is composed of the occupational records of over 147,000 persons.

The organization of the ORAU/UNC epidemiology study group is shown in my first viewgraph.

The epidemiology and biostatistics section consists of nine Ph. D.'s or M.D.'s, five predoctoral students, four M.S.'s, and three support staff. The data collection and management section has a staff of six. The death certificate retrieval office has a full-time staff of four, two of whom are professionally trained nosologists.

These sections are all dependent upon the computer science section, which is composed of three M.S. systems—analyst/programers and nine programers. The combined ORAU/UNC group has a staff complement of 35 researchers and 4 secretaries.

In the next viewgraph the composition is shown of our consultant staff; our peer review advisory committee, which has Dr. George Hutchison as chairman; the research planning group, which has oversight; the program management staffs of DOE in Germantown and Oak Ridge; and the staff designated by Union Carbide Nuclear Division to help implement this program.

The basic scientific question that our study addresses stems from national concerns about the safety of low-level radiation exposures in general. In our studies, however, this question is restated as, "Does occupational radiation exposure affect the health and mortality of radiation workers in DOE?" and "Does exposure to uranium and other metals and chemicals involved in development of nuclear materials and fuels affect the health and mortality of workers in this industry?"

Obtaining an answer to these questions is complicated by the many plant facilities involved—71—and the immense number of irradiated workers and their voluminous records, which shows in the 35 years of operation there have been almost 2 million records taken of these employees. Over in the area marked at the top "Years 5-10"—that is the rem dose per year—these are the persons above the 5 rem constraint. You can see among these 1.9 million there are 1,800 persons who have been so irradiated.

The portion of this study being conducted by Oak Ridge Associate Universities with the collaboration of the University of North Carolina is shown in the accompanying block diagram on the next viewgraph.

The central large block shows the "Oak Ridge Segment" and the six major DOE facilities that now compose it: The block called the Niagara Frontier of the Manhattan Engineer District, and the other major, early uranium processing sites are on the block at the upper left; the large narrow box extending across the diagram labeled "greater than" 5 rem indicates the across-the-industry nature of this particular study.

The arrows terminating in this box indicate the sources of the radiation-exposed and control populations involved in this study In the boxes to the right of the Oak Ridge segment are listed the facilities where plutonium exposures were a major hazard and other sites where epidemiologic studies are the major concern of others.

The block diagram shows the various phases of the standard study process used in preparing the data bases and analytical files for ORAU/UNC. The arrows show the directions of the process and how the error correction, editing, and validation of the records occur simultaneously as various phases proceed.

Phases I and II when complete result in the necessary data for vital status determination to be carried out through SSA by our death certificate retrieval office. Completion of the identification of deaths and retrieval of their death certificates allow completion of a master roster file.

Phase III of collecting and organizing the personnel files, work history files, and exposure files then proceeds. Completion of it leads to formation of an inventory file and a cross-linked analytical file.

Phase IV, obtaining and entering data from medical records, the most difficult of these tasks, is needed for final completion of the studies to control for such potential confounders as smoking, alcohol usage, genetic or familiar abnormalities.

When these data become available and the hazards assessments are complete, the data set is ready for definitive epidemiologic study and final publication. The time scale at the top of the diagram shows that the lag time from start to finish is 2 to 6 years.

At the end of fiscal year 1981 the various parts of the Oak Ridge studies were at different stages of completion. In terms of the data collection and management phases shown in figure 2, these stages were as shown in table 5.

It shows, for example, in the Niagara Frontier study we are in phase one and two, which are the preliminary phases of getting a major roster together, while down in the Oak Ridge Segment you can see that the Tennessee-Eastman Corp., we are already in publication, publications have already been in open literature.

We have published preliminary results of studies involving our Y-12 and X-10 populations. K-25 is right now in inventory file preparation, and we will have results from that quite shortly, unfortunately, for the Paducah sites, you see, are past the master roster file, but only in the work history file preparation.

As requested by the subcommittee, we have described at length in the written testimony the actions we have taken to implement the recommendations that have been made by the four committees that have reviewed our program. We stand ready to discuss these in detail, should you wish.

This concludes the oral portion of my statement.

[The prepared statement of Dr. Lushbaugh follows:]

STATEMENT OF

C. C. LUSHBAUGH, PH.D., M.D.

CHAIRMAN, MEDICAL AND HEALTH SCIENCES DIVISION

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ACTING DIRECTOR AND CO-PRINCIPAL INVESTIGATOR,

DOE HEALTH AND MORTALITY STUDIES

(OAK RIDGE SEGMENT)

CENTER FOR EPIDEMIOLOGIC STUDIES

OAK RIDGE ASSOCIATED UNIVERSITIES

BEFORE THE

SUBCOMMITTEE ON INVESTIGATIONS AND OVERSIGHT

COMMITTEE ON SCIENCE AND TECHNOLOGY

U. S. HOUSE OF REPRESENTATIVES

MAY 19, 1982

Introduction

Mr. Chairman and members of the Subcommittee, I appreciate this opportunity to provide information concerning the ongoing Department of Energy's Health and Mortality Study being conducted in part by Oak Ridge Associated Universities under my direction. I am accompanied today by Dr. Carl Shy, Professor of Epidemiology of the School of Public Health, University of North Carolina, who is co-principal investigator with me on these studies. Dr. Carl Shy is responsible for the scientific merit of our epidemiologic analyses, while I am largely responsible for the operational problems of data collection; data computerization and management; scientific staff development and organization; day-to-day establishment of working priorities, goals, and schedules.

Dr. Shy leads a subgroup of occupational epidemiologists and staff persons located at the Chapel Hill, North Carolina campus (UNC) where two of our Oak Ridge senior staff members are in residence this year. Dr. Shy will describe for you later the scientific epidemiologic problems our combined groups are addressing. I will describe the scope of the "Oak Ridge Segment" of the DOE Health and Mortality Study and the more pragmatic aspects of this program.

Group Organization

Together Dr. Shy and I have put together a well-trained group of scientists and technicians who are applying epidemiology theory and methodologies, biostatistics, computer science and programming, and modern methods of data collection and data management to overcoming the innumerable problems of studying an extraordinarily large epidemiologic data base at Oak Ridge, comprised of the occupational records of over 127,000 persons. The numbers of these records (Table 1) illustrate the almost unprecedented size of the Oak Ridge data base which requires state-of-the-art competence in its computerization and management. Our groups alone could not accomplish this task without the subcontracted support of the staffs of Computer Science Division, Union Carbide Corporation Nuclear Division, Oak Ridge, and that of the Triangle University Computation Center, Research Triangle Park, NC. The organization of the ORAU/UNC Epidemiology Study Group is shown in Table 2.

The Epidemiology and Biostatistics Section, counting both full- and part-time workers, consists of 9 Ph.D.'s or M.D.'s, 5 predoctoral students, 4 M.S.'s and 3 support staff. The data collection and management section has a staff of 6. The Death Certificate Retrieval Office (DCRO), which determines vital status of all DOE-study populations (Hanford, Los Alamos, as well as those of the "Oak Ridge Segment") and obtains their death certificates has a full-time staff of 4, two of whom are professionally trained nosologists who do all ICD encoding. These sections are all dependent upon the creative computer services of the computer science section, which is composed of 3 M. S. systems-analyst/programmers and 9 programmers. The combined ORAU/UNC group, therefore, has a staff complement of 35 researchers and 4 secretaries.

TABLE 1

NUMBERS OF RECORDS IN DATA BASE

			Individual Records
Master Roster File		=	226,000
Oak Ridge Plants Only		=	132,200
Radiation Exposure Records		=	2,082,000
Oak Ridge Only	K-25	=	370,000
	X-10	=	610,000
	Y-12	=	873,000
Total Oak Ridge		-	1,853,000
Work History			
Department Codes		=	290,000
Job Codes and Titles		=	220,000
Hire and Term		=	202,000
Total		=	712,000
Death Certificate			
Val. and Coded		=	27,000
Total DOE System		=	47,000

TABLE 2

DOE H & M STUDY

"OAK RIDGE SEGMENT"

C. C. Lushbaugh, Ph.D., M.D.

(Manager)

STAFF

Administration

- D. Robie, B.A. (ORAU)
  - F. Zenni
  - J. Jones
  - M. Freels
- S. Wolf, M.P.H. (UNC)
  - B. Seagroves

Data Collection and Management

- D. Robie, B.A. (ORAU)
- S. Taylor
- S. Owens (UCC-ND)
- R. Richmond
- S. Delcour

Death Certificate Office

- [D. Cragle, Ph.D.] (ORAU)
- T. Newport, B.A. (NOS.)
- S. Ball (NOS.)
- C. Murphy (Chief)
- D. Young

May 1982

Epidemiology/Biostatistics

- C. Shy, M.D., M.P.H., Ph.D. (UNC)
  - M. Ibrahim, M.D., M.P.H., Ph.D.
  - H. Tyroler, M.D.
  - H. Checkoway, Ph.D.
  - J. Watson, Ph.D.
- J. Smith, M.S.
- V. Manley

- S. Fry, M.B., B.Ch. (ORAU)
- D. Cragle, Ph.D.
- E. Frome, Ph.D. (UCC-ND)
- D. Hudson, M.S.
- A. Carpenter, D.D.S., M.P.H.
- W. Tankersley, M.S.
- M. Khare, M.S.
- D. Davies
- L. Sowder, B.A.

Graduate Students

- D. Cookfair, M.S. (UNC)
- J. Wilson, M.S.
- N. Abd Elghany, M.B., B.Ch.
- D. Strom, M.S.
- B. Dupree-Ellis, M.S.

Computer Sciences

- M. Wray, M.S. (ORAU)
- K. Gissel, M.S.
- I. Rosenblitt, M.S.
- K. Pearson
- S. Huff, B.S.
- D. Harmon
- M. O'Brien, B.A.
- K. Zehner, B.S.
- J. Gray
- M. Worrel (PT)

- R. Mathew (UNC)
- S. Muller

UCC-ND

- H. Fore & Staff

In Table 3 the composition is shown of our consultant staff; our peer review advisory committee, which with Dr. George Hutchison as chairman reviews our program annually; the Research Planning Group (RPG), which under the chairmanship of Professor Shy reviews all scientific protocols; the program management staffs of DOE in Germantown and Oak Ridge; and the staff designated by UCC-ND to help implement this program.

Program Objectives and Goals

The basic scientific question which our study addresses stems from national concerns about the safety of low-level radiation exposures in general. In our studies this question is restated as, "Does occupational radiation exposure affect the health and mortality of radiation workers?" While our major goal is to answer that question, a second objective has been added to answer the question, "Does exposure to uranium and other metals involved in development of nuclear materials and fuels affect the health and mortality of workers in this industry?" Obtaining an answer to these questions is complicated by the many diverse (76) facilities involved in the past and present, the immense number of workers exposed (Table 4), and the voluminous records accumulated over more than 35 years. The portion of this study being conducted by Oak Ridge Associated Universities with the collaboration of the University of North Carolina is shown in the accompanying block diagram (Fig. 1) which illustrates the relationship of the three major "Oak Ridge Studies" actively under way at this time, to other AEC/DOE facilities and DOE-supported segments of the larger study. The central large block shows the "Oak Ridge Segment" and the six major DOE facilities that now comprise it (total past and present population $\sim$140,000); the Oak Ridge-only group of 4 sites, one of which (TEC, population 40,000) is defunct (80,000); the three gaseous diffusion plants where, in addition to radiation exposure, uranium, fluorine and nickel exposures are major threats (50,000 workers); and subset of special preliminary studies which are largely exploratory and hypothesis-generating, focused on data subsets as data-base validation has proceeded. The block called "Niagara Frontier" of the Manhattan Engineer District (MED), (3200 total population of whom 2000 were Linde employees); and the other major, early uranium processing sites--Mallinckrodt (MCW) (3700), National major early uranium processing sites--Mallinckrodt (MCW) (3700), National Lead of Ohio (6600), and Middlesex (dotted lines indicating only an employment list at hand). The large narrow box extending across the diagram labeled $\geq$ 5 rem indicates the across-the-industry nature of this particular study. The arrows terminating in this box indicate the sources of the radiation exposed and control populations involved in this study. In the boxes to the right of the "Oak Ridge Segment" are listed the facilities where plutonium exposures were a major hazard and other sites where epidemiologic studies are the major concern of others. Similarly in the three boxes at the bottom of the chart DOE facilities are listed according to their major purposes--weapons, research and development and reactors. Some of these sites are listed in other boxes and illustrate in part some of the areas of overlapping interests and their involvement in several studies.

TABLE 3

DOE H & M STUDY - "OAK RIDGE SEGMENT"

(continued)

CONSULTANTS

A. Polednak, Ph.D. (NYSPH)
P. Cole, M.D., Ph.D. (UAB)
D. Cookfair, Ph.D. (RPMH)
M. Hansard, Ph.D. (CPS)
E. Dupree-Ellis, M.S. (UNC)
C. Steger, M.S. (RPMH)
M. Bremseth, Ph.D. (UT)
J. Morehead (UCC-ND)

ADVISORY COMMITTEE

G. Hutchison, M.D., Ph.D. (HU)
  Chairman
P. Enterline, Ph.D. (UP)
J. Boice, Ph.D. (NCI)
A. Furst, Ph.D. (USF)
P. Brubaker, Ph.D. (EXXON)
K. O'Kane, Ph.D. (UT)

RESEARCH PLANNING GROUP

C. Shy, M.D., M.P.H., Ph.D. (UNC)
C. Lushbaugh, Ph.D., M.D. (ORAU)
M. Ibrahim, M.D., M.P.H., Ph.D. (UNC)
J. Watson, Ph.D. (UNC)
S. Fry, M.B., Ch.B. (ORAU)
D. Cragle, Ph.D. (ORAU)

DOE-OHER PROGRAM MANAGEMENT

J. Thiessen, M.D.
J. Blair, M.D.
R. Goldsmith, Ph.D.

DOE-OR-OPERATIONS

W. Bibb, Ph.D.
R. Benson, D.V.M.

UNION CARBIDE CORPORATION NUCLEAR DIVISION

C. Richmond, Ph.D. (ORNL)
R. Jordan (Y-12 Hdq.)
H. Fore (CSD)
E. Frome, Ph.D. (CSD)

May 1982

TABLE 4

RADIATION EXPOSURE OF AEC AND AEC CONTRACTOR PERSONNEL TO WHOLE-BODY PENETRATING RADIATION

	REM DOSE				
YEARS	0-1	1-5	5-10	10-15	>15
1947-54	130,128	5,311	284	32	6
1955	56,708	3,157	285	41	1
1956	38,225	2,312	100	4	3
1957	45,510	2,424	83	5	1
1958	59,455	6,271	159	10	12
1959	71,600	3,912	66	2	1
1960	77,522	4,629	41	2	1
1961	90,651	5,174	40	3	8
1962	122,437	5,707	113	0	8
1963	107,786	5,472	80	0	1
1964	122,711	6,157	86	11	0
1965	128,360	6,671	175	8	0
1966*	131,522	6,242	167	0	2
1967*	102,510	5,767	108	1	0
1968	103,206	4,776	4	0	0
1969	98,625	4,288	4	1	0
1970	92,185	4,464	12	0	0
1971	90,640	3,661	12	1	1
1972	86,077	3,373	10	0	0
1973	89,071	2,903	3	0	0
1974	73,845	2,318	3	0	0
TOTAL	1,918,774	94,989	1,835	121	45

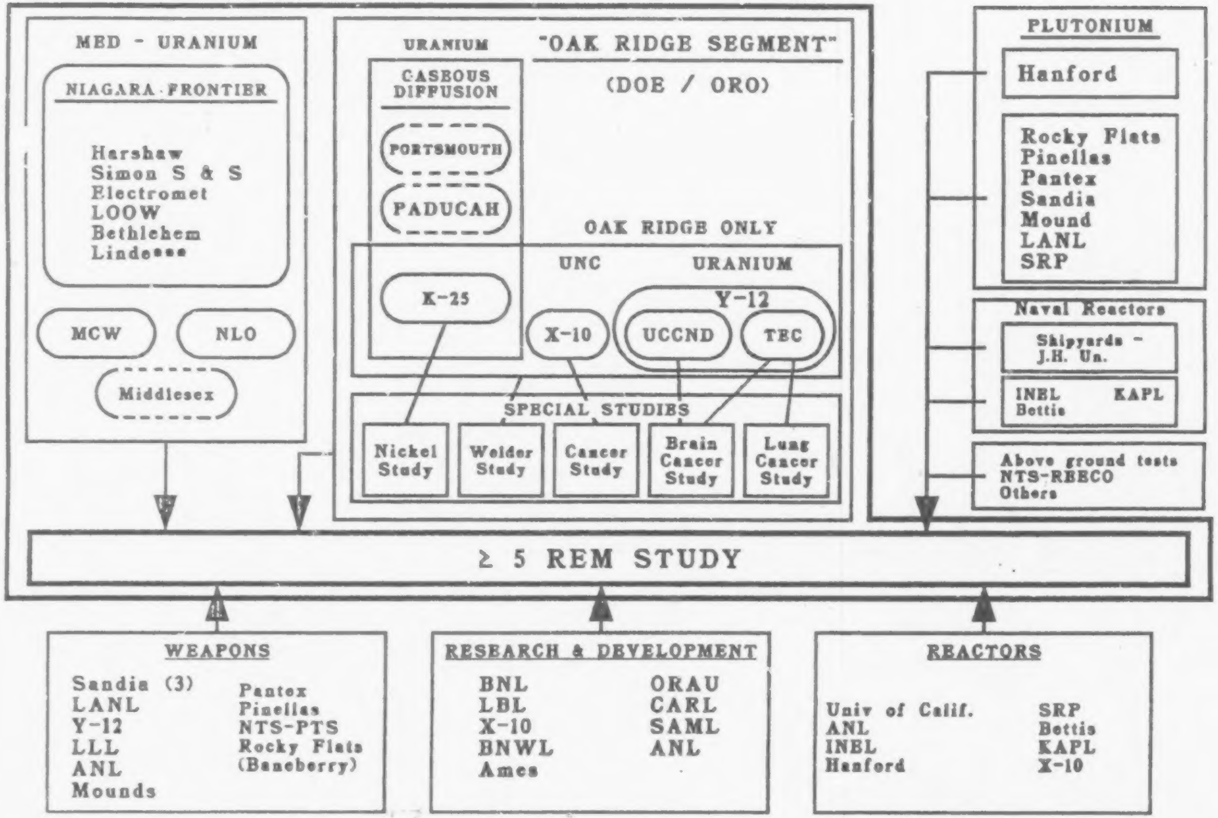
*Totals for 1966 and 1967 differ from those shown in previous editions of this publication, due to the discovery of an error in the radiation exposure records of one major contractor.

SOURCE: "Operational Accidents and Radiation Exposure Experience within the United States Atomic Energy Commission, 1943-1975." (WASH 1192), USAEC, Division of Operational Safety, Washington, D.C., 1975, p. 10.

NOTE: This table includes the number of recorded exposures at specified levels; of course, the number of persons exposed cannot be readily determined since longer-term employees will be included in the data for several years.

FIGURE 1

DOE HEALTH & MORTALITY STUDIES



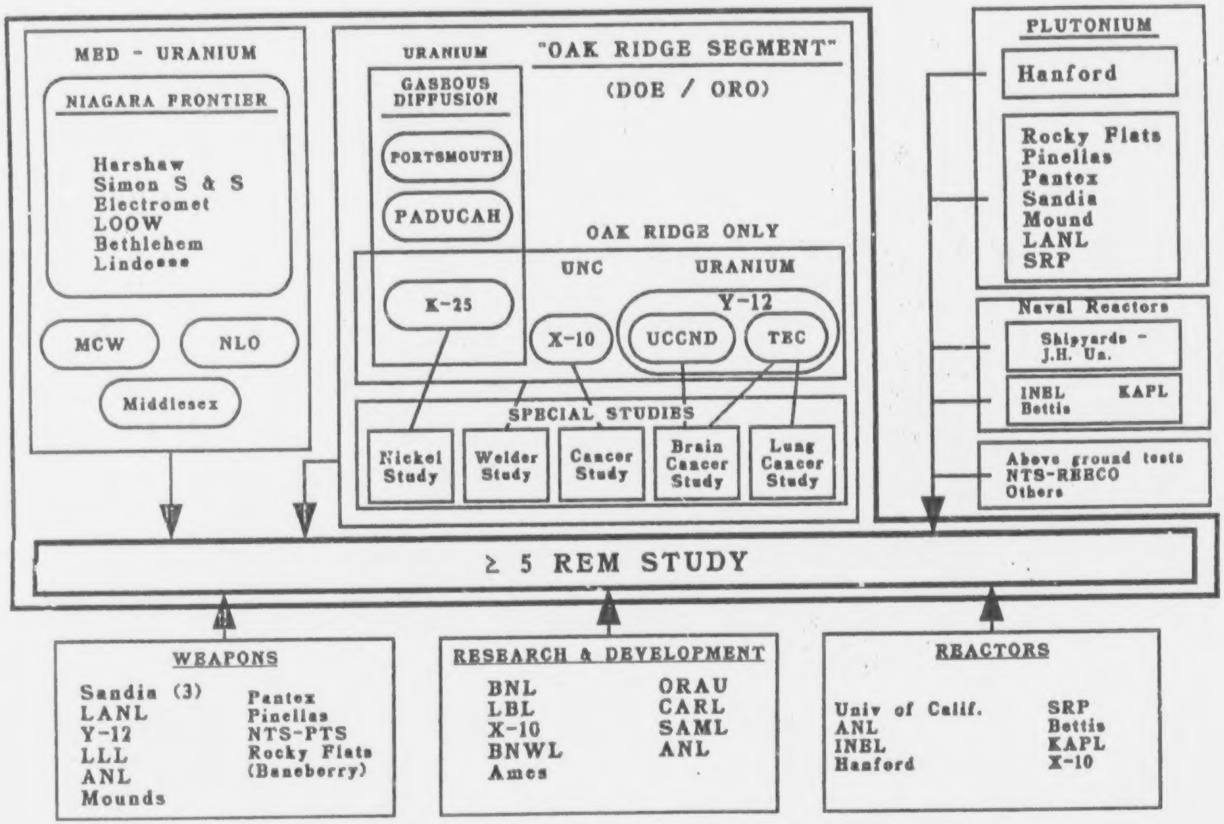
MED - URANIUM
NIAGARA FRONTIER
Harshaw
Simon S & S
Electromet
LOOW
Bethlehem
Linde***
MCW
NLO
Middlesex
URANIUM
GASEOUS DIFFUSION
PORTSMOUTH
PADUCAH
"OAK RIDGE SEGMENT"
(DOE / ORO)
OAK RIDGE ONLY
UNC
URANIUM
Y-12
K-25
X-10
UCCND
TEC
SPECIAL STUDIES
Nickel Study
Welder Study
Cancer Study
Brain Cancer Study
Lung Cancer Study
PLUTONIUM
Hanford
Rocky Flats
Pinellas
Pantex
Sandia
Mound
LANL
SRP
Naval Reactors
Shipyards - J.H. Un.
INEL
Bettis
KAPL
Above ground tests
NTS-REECO
Others
≥ 5 REM STUDY
WEAPONS
Sandia (3)
LANL
Y-12
LLL
ANL
Mounds
Pantex
Pinellas
NTS-PTS
Rocky Flats
(Baneberry)
RESEARCH & DEVELOPMENT
BNL
LBL
X-10
BNWL
Ames
ORAU
CARL
SAML
ANL
REACTORS
Univ of Calif.
ANL
INEL
Hanford
SRP
Bettis
KAPL
X-10

The three high-priority studies that comprise the major concerns of the Oak Ridge-ORAU-Center for Epidemiologic Studies and its University of North Carolina collaborators are delineated on this diagram within a single larger box: 1) the Oak Ridge Segment, 2) the Niagara Frontier MED sites, and 3) the $\geq$ 5 rem study.

Organization of the Study Process

The block diagram (Fig. 2) depicts the various phases of the standard study process used in preparing the data bases and analytical files for ORAU/UNC. All protocols are designed to produce publishable reports of a definitive, specific epidemiologic study of a DOE facility's health and mortality experience, which can be merged later into an analysis containing as many workers as feasible. The arrows show the directions of the progress and how the error correction, editing, and validation of the records occur simultaneously and repetitively as the various phases proceed in or out of phase with others, depending on record availability and completion of various steps by others such as Social Security Administration (SSA), Death Certificate Retrieval Office, State Departments of Vital Statistics, etc. Collection Phases I and II when complete result in the necessary data for vital status determination to be carried out through SSA by our Death Certificate Retrieval Office. Completion of the identification of deaths and retrieval of their death certificates allow completion of a master roster file which can be explored analytically to see whether the data contain information usable for hypothesis generation, changing priorities or identifying problems needing immediate correction. As the master roster file data are being edited and validated, Phase III of collecting and organizing the personnel files, work history files and exposures files is accelerated. Completion of this set of files leads to formation of an inventory file which in its simplest use shows the commonality of the information for individual workers and allows frequency distribution analyses to be done so that design of analytical protocols can proceed. Completion of the experimental design provides guides for linking the data to provide a cross-linked analytical file from which data can be obtained for specific analyses to test hypotheses such as, for example, "four years of respiratory exposure to uranium dust does not result in an increased mortality from respiratory disease." Phase IV, obtaining and entering data from medical records, the most difficult of these tasks, is needed for final completion of the studies to control for such potential confounders as smoking, alcohol usage, genetic or familial abnormalities. When these data become available and the hazards assessments are complete, the data set is ready for definitive epidemiologic study and final publication. The time scale at the top of the diagram shows the "lag" time from start to finish is two to six years. This long lag time prevents our doing studies of individual populations consecutively and forces their concurrent development and study. Because delays cannot always be avoided, data from a facility of lesser programmatic interest can become ready for study before analytical files are completed of the records of higher priority sites. At first glance, such occurrences suggest that fragmentation of the

DOE HEALTH & MORTALITY STUDIES


MED - URANIUM
NIAGARA FRONTIER
Harshaw
Simon S & S
Electromet
LOOW
Bethlehem
Lindesse
MCW
NLO
Middlesex
URANIUM
GASEOUS DIFFUSION
PORTSMOUTH
PADUCAH
K-25
"OAK RIDGE SEGMENT"
(DOE / ORO)
OAK RIDGE ONLY
UNC
URANIUM
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PLUTONIUM
Hanford
Rocky Flats
Pinellas
Pantex
Sandia
Mound
LANL
SRP
Naval Reactors
Shipyards - J.H. Un.
INEL
Bettis
KAPL
Above ground tests
NTS-REECO
Others
≥ 5 REM STUDY
WEAPONS
Sandia (3)
LANL
Y-12
LLL
ANL
Mounds
Pantex
Pinellas
NTS-PTS
Rocky Flats
(Baneberry)
RESEARCH & DEVELOPMENT
BNL
LBL
X-10
BNWL
Ames
ORAU
CARL
SAML
ANL
REACTORS
Univ of Calif.
ANL
INEL
Hanford
SRP
Bettis
KAPL
X-10

whole study is occurring, whereas they are reflective of unavoidable delays in the study process. These smaller studies provide pilot tests which help refine procedures for use in analytic data collection procedures in the larger populations. At the end of FY 1981 the various parts of the Oak Ridge studies were for these reasons at quite different stages of completion. In terms of the data collection and management phases shown in Fig. 2 and described briefly above, these status were:

TABLE 5

Present Phases of "Oak Ridge" Study Progress 1982

Studies	Phases
1. Niagara Frontier (6)	I & II*
Mallinckrodt	III + Presentation 1
National Lead of Ohic	IV + Presentation 1
2. $\geq$ 5 rem	II & III
3. Oak Ridge Segment	
TEC	AF** Publication 1
Y-12	AF Presentation 2
X-10	AF Presentation 1
K-25	IF/AF + Special Studies
Portsmouth	III
Paducah	III

---

* I & II = master roster being formed

** AF = analytical file

IF = inventory file

Note: See also appended bibliography.

Summary of Research Progress FY 1982 at ORAU/UNC

1. Y-12 Plant [Tennessee-Eastman Corporation (TEC), Oak Ridge]

Data collection and lung-dose calculations were completed for the lung cancer case-control study. A detailed evaluation of chemical exposures and their connection to work-history data was completed. An analysis file to include this information and to update mortality in the entire population through 1977 was created. A case-control study of brain cancer deaths that occurred between 1948 and 1977 in the entire cohort was initiated. This study will investigate the effects of exposure to uranium dust and to chemicals such as trichloroethylene, carbon tetrachloride and nitric acid. A feasibility study for analysis of the large group of female workers (19,000) employed at Y-12 between 1943 and 1947 was completed. A preliminary proportional mortality ratio (PMR) analysis indicated a possible increase in respiratory diseases, particularly pneumonia, and in lymphopoietic cancer, brain cancer, cancer in the uterus, cervix and skin. This PMR study contained only deaths that occurred before the end of 1973. The data set has now been updated through 1977 and is in process of being reexamined. Even though the follow-up in the women is more difficult, and less complete than the follow-up in the men, methodologic research in this area indicates that case-control studies of the women can be made to yield valid results and need to be carried out.

2. Y-12 Plant (UCC-ND, Oak Ridge)

A thorough exploratory analysis of the Y-12 preliminary file was performed in order to examine some of the effects of length of employment, age (i.e., pre- and post-retirement), and internal as well as external radiation exposure. Since the "healthy worker effect" is always a concern, only employees who worked at least 6 months were included in the analysis in an attempt to remove any "transient worker" effects. The resulting cohort consisted of 6400 white males of whom 565 were identified as dead and 425 were of unknown vital status. Death certificates of 532 (94%) were retrieved successfully and coded for underlying cause of death.

Significant standardized mortality ratios (SMR) ($p<.05$) were observed for brain cancer only in individuals employed 5 to 10 years (SMR = 5.89, deaths = 6) and leukemia and aleukemia only in individuals less than 40 years old (SMR = 10.37, deaths = 2). The SMR was close to significance for brain cancer in 40 to 65 years old (SMR = 2.17, deaths = 8). A positive trend with age appears to be present in the SMR's for lung cancer while a negative trend is present for circulatory diseases. In looking at length of employment, the trends are consistently negative for lymphatic tissue cancers and respiratory diseases.

The major radiation hazard at the Y-12 plant in the past is conceived as being most likely internal radiation exposure of the lungs. However, a comparison of lung cancer SMR's in individuals monitored for internal exposure and those not so monitored (no risk?) showed only a possibly positive trend test (.89 vs 1.13). A Poisson rate analysis of the data resulted in an estimated relative risk for lung cancer in the monitored group of 1.34 but with a 95% confidence interval of (.74, 2.46).

3. Oak Ridge National Laboratory (UCC-ND)

Two epidemiologic studies are being conducted on the X-10 cohort at this time. The first is a retrospective cohort, mortality study in which the mortality experience of X-10 workers is being contrasted with that of the general U. S. population for the years 1943-77. The second is a case-control study comparing the radiation and chemical exposure histories of all cancer deaths with controls obtained from the cohort.

A cohort of 8717 white males who worked for at least one month between 1/1/43 and 12/31/74 at X-10 has been identified for the first study. These are persons who did not work at any other DOE facility. Vital status follow-up on this cohort is being conducted. As of this writing, vital status has been determined for 88% of the cohort and death certificates have been obtained for roughly 95% of the known deaths. The data tapes containing external radiation dosimetry and work history information have been edited and validated and are being linked with the demographic and vital status data for analysis. The data tape containing internal radiation exposure information is still being edited and errors being corrected.

Approximately 420 cancer cases and 840 controls have been selected from the X-10 cohort for the second study. The computer files containing work history, external radiation, and metal exposure data have been prepared.

4. Oak Ridge Gaseous Diffusion Plant (UCC-ND), K-25

The K-25 data inventory file was completed and contains records for approximately 43,900 individuals; one record per individual provides information on the kinds of data available for each individual prior to analysis file construction. This file also furnishes information on missing or incomplete data, and is used as a tool for error detection and correction as well as for making informed decisions concerning the structure of future K-25 analysis files.

5. Oak Ridge Welders Study

Mortality and causes of death were studied for a cohort of 1302 white male welders employed at the nuclear facilities in Oak Ridge between 1943 and 1977. Deaths reported as of mid-year 1979 were used in standardized mortality ratio (SMR) analyses. For the entire cohort the SMR for all causes of death was 0.98 with a 95% confidence interval (c.i.) of (0.87, 1.11) and 1.26 (5% c.i. = 0.80, 1.89) for lung cancer. The SMR for respiratory disease (ICD 460-519) showed an increasing excess in mortality at 1.55 (95% c.i. = 0.97, 2.34) when compared to an earlier published study where the SMR was 1.33 (95% c.i. - 0.71, 1.60). The growing excess found appears to be due to emphysema, a cause of death found to have a significantly high SMR of 2.61 (95% c.i. = 1.25, 4.79) in this occupation. When looking at the subgroup of welders exposed to nickel oxides at the K-25 plant, no significant increases in mortality were found for any disease.

The increase in respiratory diseases being found is occurring in the non-K-25 welders in Oak Ridge.

Analysis of the four Oak Ridge facilities appears to show that welders who worked at the Tennessee Eastman Corporation (TEC) between 1943 and 1947 have an SMR of 2.56 (95% c.i. = 1.23, 4.72) for respiratory disease based on ten observed deaths. In order to try to equalize follow-up time, welders hired in Oak Ridge before 1955 were analyzed by facility (K-25, Y-12, X-10, TEC). This analysis showed results similar to those of the study of only TEC welders where a significant excess mortality due to respiratory diseases was found.

6. Oak Ridge Facility Comparison Study (ORFCOM)

The analysis file which will be built in this study is envisioned as a biostatistical resource for all the DOE Health and Mortality Studies. From it death rates are being generated for the entire white male Oak Ridge worker population since 1943. These rates for the total white male Oak Ridge worker population will provide a comparison standard for the K-25, X-10, and Y-12 studies. Use of this comparison standard should eliminate the problems being encountered as comparisons are made of groups of healthy workers with the overall U. S. or Tennessee populations which per force contain workers who terminated from all industries because of ill health. The ORFCOM file now includes 72,814 white males who ever worked at any of the Oak Ridge plants (TEC, K-25, Y-12, X-10) through the end of 1977. The file contains facility, date of first hire and last termination, vital status, date of birth, date of death, and cause of death (where appropriate). Death certificates coded for the underlying cause of death were available for 88.5% of the 20,189 deaths identified by the Social Security Administration.

7. Mallinckrodt Chemical Works

Reentry of the employee film-badge data was completed. Efforts to increase the percentage of vital status determination were intensified. All white males whose vital status was unknown were sent to the Department of Motor Vehicles of Missouri and Illinois and were searched for on the Missouri death index. The development of this search method has helped resolve the vital status for 32% of "status unknowns."

8. Manhattan Engineering District

Rosters were developed and submitted to SSA for Linde, Harshaw, Lake Ontario Ordnance Works, Simonds Saw and Steel, and Electrometallurgical Laboratory. Film badge data, medical examinations, and serial blood and urinalyses were located for a number of the workers at these facilities. The goal is to have an exploratory analysis completed by mid-FY 1982.

9. DOE $\geq$ 5 Rem Study Registry

The initial phase of data collection was completed in FY 1981 for the present and former employees reported to have received $\geq$ 5 rems during at least one year of employment at 40 of the 76 surveyed sites of DOE, DOE contractors, or DOE's Naval Reactor Program. This study population now consists of 3146 individuals. Alternate methods have, thus far, been successful in determining the vital status of 418 of the 856 persons whose vital status was not determined by the Social Security Administration (SSA). These methods, that include follow-up by states' Motor Vehicle/ Drivers' License Departments, are being systematized by the Epidemiology Group, M&HSD, to facilitate the follow-up of larger numbers of "unknown" in the Health and Mortality Study populations. DCRO has obtained, verified, and coded (underlying cause of death, 8th Revision ICD) death certificates for 193 of the 338 individuals known to be dead. Data to aid in verification of an additional 88 certificates on-hand are being obtained from PSQ's stored locally or in Washington, DC. A very preliminary SMR analysis based on 55% death certificate ascertainment for 289 deaths among white males in the population, using the age adjusted mortality rates of the U. S. white male population for comparison, showed no excess mortality due to all causes (SMR = 0.71). SMR's $\geq$ 1.00 were obtained for mental disease (1.00), chronic nephritis (1.03) and cancers of the stomach (1.08), rectum (1.28), liver (1.49), larynx (1.55), and esophagus (1.54); none of the values was statistically significant. However, given the small number of cases in each of these categories and the incompleteness of the data at that time, no conclusions can or should be drawn from these results.

Our previous progress toward the goals of this study is illustrated in part by the unselected bibliography which is appended.

This bibliography lists 14 articles in peer reviewed journals; 14 abstracts, and 13 articles in proceedings and symposia. These report the various stages of the development of needed methodologies and the results of these studies as they were produced.

Part III

ACTION RESPONSES TO PEER REVIEW RECOMMENDATIONS - 1980 and 1981

1. Full-time scientific leadership problem.

   a) Developed: University of North Carolina contractural relationship; Dr. Carl Shy (Professor of Epidemiology) as Co-Investigator with Dr. Lushbaugh; Drs. M. Ibrahim and H. Tyroler (Professor of Epidemiology) as Research Program Group (ORAU/UNC) advisers; regular RPG meetings with formal review of all proposals and protocols; active interchange of UNC and ORAU staff and advanced students.

   b) Continued to improve Oak Ridge project management structure for data collection, management and analysis by recruitment of on-site epidemiology Ph.D.'s, M.S.'s and M.P.H.-trained physicians. -D. Cragle, Ph.D. (UNC), S. Fry, M.B., Ch.B., M.P.H. (UNC), A. Carpenter, D.D.S., M.P.H. (UAB), E. Dupree-Ellis, M.S. (on Ph.D. training leave at UNC); J. R. Qualters, M.S. (U. Mich.) (in hiring process May 1982).

   c) Recruitment to project at Chapel Hill site (UNC) of Assist. Prof. Harvey Checkoway, Ph.D. as lead Epidemiologist under Dr. Shy.

   d) Recruitment of Philip Cole, M.D., Ph.D., University of Alabama (Birmingham) as consultant in Human Oncology and Cancer Epidemiology.

   e) Appointment (effective June 1982) of S. Fry, M.B., Ch.B., M.P.H. as Oak Ridge on-site group leader, replacing C. C. Lushbaugh, Ph.D., M.D., acting ORAU group leader 1980-1982.

2. The need to develop an overall study plan directed at a coordinated interpretation of the data from all occupational groups under study is being met under the direction of the DOE Office of Health and Environmental Research (Drs. J. Thiessen and R. Goldsmith) (See Figures 1 and 2.) ORAU/UNC have assigned priorities for study of:

   a) The Niagara Frontier - Manhattan Engineering District uranium processing facilities (6 in Buffalo, NY area, one each in St. Louis, MO., Cincinnati, OH, and Middlesex, NJ). There will be no problem in obtaining a finally integrated study but preliminary exploratory studies are needed for the three most populous of these sites first, to assure the availability and completeness of validated population rosters and exposure records. Highest priority in these tasks is being given to the Linde Air Products (Union Carbide Corporation) Division site at Tonawanda, NY.

   b) The so-called "Oak Ridge Segment" of the DOE Health and Mortality Studies which for Oak Ridge Only includes the UCC-ND facilities called K-25, X-10, Y-12, and Tennessee Eastman Corporation Y-12 facility. Additional facilities, not under active study because of incomplete data collection and the comparatively recent operations of these facilities, are: the uranium enrichment plants at Paducah, KY, and Portsmouth (Piketon), OH.

These individual site studies will ultimately be integrated in a single study of uranium enrichment by gaseous diffusion (K-25, Paducah, and Piketon) while the Oak Ridge sites will be integrated into a single ∿80,000 person population (about 40,000 white males) to avoid the biases of geography, the healthy worker, and local medical quality; all common complications of analyses that use U. S. Vital-Statistics-at-large for comparison.

c) The "≥ 5 rem study" focuses on the question of the safety of a 5 rem/annum radiation exposure constraint imposed by DOE on its atomic workers. The 3200 such persons worked or are working at 40 of the 76 facilities involved where 6400 controls are being sought. The "integration" suggested by the committee as a needed part of its experimental design is a required feature of this study.

3. As suggested for improving exchange of information between DOE epidemiology project sites various group members have served as observers at the site visits of peer review committees at Hanford, Los Alamos, Argonne. The recently held Rockville DOE workshop on Radiation Epidemiology was an immense help in further development of intergroup collaboration and cooperation.

4. Our efforts to verify study population lists have been expanded by organizing a subgroup of 5 persons (see Table 2) under Ms. Shirley Taylor, an expert in data management and location of missing and unknown persons, trained at and previously employed by the Department of Epidemiology staff at UNC; by additional microfische readers and microfilming equipment; and continuing education and training of the group at national training centers and symposia.

5. The radiation dosimetry studies have developed a standard radiation assessment protocol for use at all DOE sites presently under study. This protocol is available to the subcommittee. This effort was also directed by our need to expedite the "≥ 5 rem Study" which requires matching controls and their radiation dosimetry from 40 of the 76 former AEC/ERDA/DOE R & D sites.

6. The "outcome activity" has been expanded and its efficiency enhanced by our success in obtaining 29 of the 50 U. S. state death tapes. The ones where we have been unsuccessful so far are legally protected for privacy reasons from our possession (but not from our continued indirect use). We were successful in 1982 in obtaining the aid of 23 state auto vehicle operators licensing bureaus. This (not inexpensive) assistance has so far proven to be quite rapid and at last count to have helped us resolve 35 percent of our "vital status unknowns". See Tables.

7. ORAU personnel department was able to improve computer science salaries by a job market analysis as the result of this recommendation.

8. The appended bibliography for the ORAU/UNC epidemiology group's output of scientific articles, etc. reveals that multiple authorship with full acknowledgement of all persons involve is established policy. Whereever a person's efforts are routine, service-directed and not directly contributory to the scientific effort, this person's involvement is acknowledged by footnote.

9. The four major section leaders involved in management of our data base

Part III (continued)

TABLE 1

DEATH INDEX INVENTORY

STATE	TOTAL PERIOD	COMPUTER TAPE	MICROFICHE	MICROFILM
Alabama	1908-1980	1960-1980	1960-1980	1908-1969
Arizona	1940-1980	1970-1980	1940-1980	
California(1)	1960-1980		1960-1980	
Connecticut	1959-1977		1959-1977	
Delaware	1939-1979			1939-1979
Florida	1940-1978		1940-1978	
Georgia	1919-1979		1919-1979	
Kansas	1971-1979		1971-1979	
Kentucky	1963-1977	1963-1977	1963-1977	
Louisiana	1975-1978	1975-1977	1975-1977(2)	
Maine	1960-1980	1960-1980	1960-1980	
Massachusetts	1969-1978	1969-1978	1969-1978	
Michigan	1969-1979			1969-1979
Mississippi	1958-1978	1958-1978	1958-1978	
Missouri	1943-1980	1954-1980	1943-1953	
Montana	1954-1977	1954-1977	1954-1977	
New Jersey	1957-1979	1957-1979	1957-1979	
Nevada	1964-1978*		1964-1978	
New Mexico	1940-1980*			1940-1980
North Carolina	1975-1979	1975-1977	1975-1979	
North Dakota	1972-1977	1972-1977	1972-1977	
Ohio	1956-1980	1956-1980	1956-1980	
Tennessee	1949-1979	1949-1979	1949-1979	
Texas	1964-1980		1964-1980	
Virginia	1945-1980			1945-1980
Wisconsin	1940-1980**	1959-1980 (excl. 1969)		1940-1958 an 19
Wyoming	1940-1979		1978-1979	1940-1977
Total: 27				

*Includes copies of death certificates

**Except 1969 < 1940-1958 and 1969 on microfilm
1959 through 1980 except 1969 - on tape

(1) Purchased in March 1982

(2) PO C24705 update requested

Washington State - now in progress

TABLE 2

23 of 50 STATES PROVIDE DRIVERS' LICENSE SEARCHES TO DETERMINE VITAL STATUS OF UNKNOWN FORMER DOE WORKERS

CALIFORNIA
COLORADO
CONNECTICUT
HAWAII
IDAHO
ILLINOIS
INDIANA
MARYLAND
MASSACHUSETTS
MICHIGAN
MISSOURI
NEVADA
NEW HAMPSHIRE
NEW MEXICO
NEW YORK
OREGON
OHIO
PENNSYLVANIA
RHODE ISLAND
SOUTH CAROLINA
TENNESSEE
VIRGINIA
WISCONSIN

and analytical files attended 6 national and international conferences on "Very Large Data Bases", "System 1022 Users Conference" and "SAS Users Group" International Conference and Association for Computing Machinery during 1980 and 1981. This attendance and participation is continuing in 1982.

10. A second nosologist has been obtained to strengthen our expertise in ICD coding and their revisions VII, VIII and IX. SNOP coding is under review.

11. We are actively engaged in investigation of methodologic questions and developing solutions that are contributing to the precision of epidemiologic analyses. The research areas involved are: occupational surveillance, radiation dosimetry, data management, statistical methods, chemical carcinogenesis, multiple causalities and perception of hazard.

12. Consultants in Industrial Toxicology are now James Morehead, B.S. (Chemistry), Former Head Industrial Hygiene Y-12; Prof. John Hickey, Ph.D., UNC, Environmental Science, School of Public Health; Craig Steger, M.S., Roswell Park Memorial Institute. Further recruitment of toxicological expertise as advised by Dr. Brubaker awaits our development of sufficient toxicological files to warrant consultation at the academic level. The present effort is upon data collection from masses of handwritten unextracted data from the major Oak Ridge production plants.

In the 1981 review, two suggestions in addition to the 1980 ones to which we have been able to respond are:

4. Improved efficiency identified as needed in our computer effort is being guided by our consultant in this field, Dr. Martha Hansard whose report of March 1982 is attached.

6. The mechanism of proposal and protocol review has been formalized as suggested. All 14 protocols were revised and rewritten in FY 1982, criticized by the Research Planning Group under UNC and then approved. These protocols are available on request.

In this statement I attempt to provide the subcommittee with information which I believe is basic to the Committee's assessment of the quality of the ORAU/UNC epidemiology study group, its organization and operations and its progress to date in conducting the Oak Ridge Segment of the DOE Health and Mortality Study. This concludes my testimony. I will be pleased to answer questions.

C. C. Lushbaugh, M. D.

5/19/82

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Mr. GORE. Thank you very much. We will withhold questions until the panel is complete.

Dr. Shy.

Dr. SHY. Thank you.

In my presentation I am going to focus on the objectives of our study and talk about the role of the University of North Carolina in these studies.

Our studies are addressing three research questions which constitute our main study objectives:

One, is there any mortality excess among DOE workers?

Two, do DOE workers have more cancer than predicted, based on current radiation dose response models?

Three, are certain DOE jobs or work environments, particularly those having exposure to higher levels of occupational levels, at increased risks of death from cancer?

I propose to discuss the significance of these research objectives, mention some of the problems we encounter in trying to answer these questions, and suggest some ways in which needed epidemiologic research on occupational hazards in DOE facilities could be facilitated.

Is there any mortality excess among DOE workers? This question might well be called the "bread and butter" of occupational epidemiology. To answer it, we typically reconstruct the employment roster of a facility as of 20 or more years ago, find out who is alive or dead as of a predetermined cutoff date, say 1980, calculate death rates for major cause-of-death categories, and then compare these observed numbers of deaths with the number that would be expected if the study population had the same mortality experience for each cause as the U.S. population of the same age and time period.

The ratio of observed deaths in workers to that expected is called the standardized mortality ratio, or SMR. A cause-of-death specific SMR significantly, in a statistical sense, greater than one means, for that cause, the working population has a worse mortality experience than people of the same age and time period in the general population.

Typically, working populations have SMR's significantly less than one because, on the average, people who enter the work force have better health and experience lower mortality up to age 65 years than does the general population. This is so because the general population includes a significant proportion of disabled, unemployed or otherwise unemployable people whose life expectancy is well below average. This phenomenon is called the "healthy worker effect."

What, then, is the value of an SMR and of this entire approach to occupational health hazards?

First, the SMR give us the first indications whether within an industry there is a mortality excess among any of a sizable list of causes of death. Thus, asbestos workers early on showed a significantly elevated SMR for all cancers and for lung cancer in particular. Uranium miners showed similarly increased SMR's for lung cancer.

Second, SMR's are relatively straightforward, well standardized methods to make a preliminary evaluation of prior cancer risks in an industry.

Unlike studies of animals exposed to carcinogens in the SMR study we can investigate thousands of exposed study subjects who feed, clothe, and shelter themselves, seek medical help when seriously ill, and behave generally humanely to each other.

Thus, we can detect as significant, cancer risks at very low exposures, such that only 1 in 1,000 exposed workers are at risk of getting cancer due to the occupational environment.

Similar experiments on animals would require enormous numbers of animals maintained for their lifetime to uncover such low risks, and even then only one concentration of one chemical could be evaluated at a great cost, and we would still have to face the severe problem of extrapolating these results to humans.

There are problems in conducting occupational SMR studies, and some of these could be reduced by administrative changes at the Federal level.

First, it is costly and tedious to determine whether a person known to be alive and employed 20 or 25 years ago has survived to the present. Until recently—1979 to be exact—we had no central registry of deaths in the United States.

Routinely we must submit a list of names and social security numbers of our study group to the Social Security Administration, who can then tell us whether a death claim was filed for the listed person, whether he is still paying to or receiving funds from social security, or is inactive and thus lost to followup.

If a death claim was filed, we have to search for the death certificate in the last known State of residence and often in adjacent States. This process typically takes 1 to 2 years to obtain data on 90 to 95 percent of the original list.

This procedure could be facilitated in many ways for bona fide public health researchers: (1) IRS could be allowed to state when the last income tax statement was filed for each person on a list; and (2) mortality files from all 53 State and Territorial death registries could be centralized and alphabetized for each year for the past 40 years.

While this would be a prodigious task, in the longrun it would greatly reduce the cost of epidemiologic studies of mortality rates by industry and geographic area. In effect, the National Death Index, which begins with deaths in 1979, is performing this task but the results will be useful primarily for the next generation of epidemiologists, for whom deaths over the 20 to 40 year interval after 1978 will be the object of study.

The second manageable problem that could be addressed is that of the healthy worker effect. If the National Center for Health Statistics, in cooperation with the Social Security Administration, kept a continuing surveillance on the vital status of a small probability sample—a running sample—of the work force, epidemiologists could make comparisons of the mortality of any specific working population with this national sample of the work force.

Thus, any excess or deficit in observed mortality of a specific industry would be inherently corrected for the healthy worker effect. In particular, we would be better able to evaluate the occupational contributions to heart disease, which typically has significantly low SMR's when the general population is used as a comparison group.

Are certain DOE jobs or work environments, particularly those having exposure to higher levels of occupational chemicals, at increased risk of death from cancer? This question is the most difficult of the three to answer satisfactorily. To do so, we must characterize not only radiation but also chemical exposures of the workers at Oak Ridge.

Unlike radiation, chemical exposures are not monitored routinely, the number of chemicals utilized in many industrial processes is large, and exposure to chemicals cannot be simply reduced to a common unit of measurement. However, the health assessment of chemical hazards to DOE workers is extremely important.

Many chemicals used in the nuclear fuel cycle have greater potential for toxicity and carcinogenicity than could be expected from ionizing radiation at occupational limits of exposure.

The enrichment and processing of nuclear materials requires the use of these chemicals and, therefore, we should be at least as concerned about the exposure of workers to chemicals as to radiation at DOE facilities.

On an a priori basis, it would be reasonable to expect more cancer and other adverse health effects among DOE workers attributable to chemicals than radiation.

As a first step, one that does not require characterizing the chemical exposure of every worker, we divide the workers in a facility into functional groups based on the particular industrial process or simply on the department in which a worker was usually employed.

Age-adjusted mortality rates are then calculated for each functional group or department and compared with the average rate for the entire facility. These results often give clues that certain work environments may be associated with increased mortality rates.

The next step is to select chemicals or groups of chemicals that are known to be toxic or potentially carcinogenic and assign an exposure rank to each job for each selected chemical.

The mortality experience of workers on the high end of the exposure index can then be compared with those on the low end, or a case control study can be performed in which the cumulative exposure index of all persons dying of a specific disease, say lung cancer, is compared with persons not dying of this disease but matched with cases on age, age at hire and year of hire.

These analyses begin to pinpoint whether there are particularly hazardous chemical environments within a facility and suggest what chemicals or groups of chemicals may be responsible for the hazard. They take into account the fact that a worker may change job assignments 10 or 12 times and may be exposed to different combinations of chemicals in each job.

To evaluate these complex chemical environments by relying on animal models would be prohibitively costly and infeasible in practice. The epidemiologic approach is the only proven method for detecting chemical occupational health hazards as they typically occur in an industrial environment.

Thus, although several scientific bodies have suggested careful limitation and selection of epidemiologic studies involving low levels of ionizing radiation, largely because of statistical requirements for very large study populations, this limitation should not apply to the broader occupational health assessment of groups involved in the nuclear fuel cycle, since we know exceedingly little about the health and mortality risks of the total occupational environment, chemical as well as radiological in the nuclear industry.

Epidemiologic studies of DOE occupational health risks, particularly risks due to chemicals, deserve a high priority precisely because hazardous chemical exposures, when identified, can often be controlled by economical industrial hygiene measures.

Lastly, our role, that of the University of North Carolina, is in the main twofold: one, to bring added scientific credibility to the results of this overall project; and two, to provide the intellectual stimulus that is added to a project by involving doctoral students, their doctoral faculty committee and the faculty researchers themselves.

Concerning scientific credibility, I do not believe that Federal agencies or DOE laboratories lack scientific credibility, but there are critics of Government research who claim that bias inevitably creeps into a study when the Government studies itself or the consequences of its activities.

Such bias is not, of course, peculiar to governmental activity and, in reality, the Government research unit has nothing to gain and much to lose if it produces a biased negative evaluation.

However, the expectation of the charge of bias was good reason for the ORAU to seek collaboration with a nongovernmental research unit.

I wish to assure this committee that we, as a university, are given ample opportunity to review and critique all of the work that results from this project. In carrying out our review function, we are not acting as external advisers to the ORAU research staff but as collaborators in the earliest design phases through data analysis and writing of reports. The exchange of ideas and personnel has been continuous and substantive.

A question that may be foremost to this committee is: Should the health and mortality study of DOE facilities continue as presently structured? In my opinion, though biased, the answer is a strong affirmative, not for social or political reasons—that is, to answer those who claim much greater risks of radiation-induced mortality than present dose-response models indicate—but for the scientific and public health objectives related to the chemical and overall occupational health concerns for workers in the nuclear industry.

As I have argued, compared with our knowledge of radiation health effects, we know relatively little about the health consequences of exposure to most occupational chemicals, and exposure to these chemicals is an inherent part of employment in the nuclear industry.

Thank you, Mr. Chairman.

[The prepared statement of Dr. Shy follows:]

RESEARCH OBJECTIVES AND UNIVERSITY COLLABORATION IN THE HEALTH AND MORTALITY STUDY OF DEPARTMENT OF ENERGY CONTRACT FACILITIES

BY

CARL M. SHY, M.D., DR.P.H.*

For presentation to the U.S. House of Representatives Committee on Science
and Technology, Subcommittee on Investigations and Oversight
Washington, D.C., May 19, 1982

*Professor, Department of Epidemiology, School of Public Health
University of North Carolina at Chapel Hill, Chapel Hill, N.C., 27514

Mr. Chairman and Members of the Subcommittee, I am Carl Shy, a physician and epidemiologist on the faculty of the Department of Epidemiology, School of Public Health, University of North Carolina. I am the principal investigator for the University's collaborative study with Oak Ridge Associated Universities of the health and mortality of Department of Energy workers included under the Oak Ridge project. I have been involved in occupational/environmental epidemiology at the University for the past eight years, and prior to that I conducted environmental epidemiologic studies as an employee of the Environmental Protection Agency.

In my presentation today, I wish to focus on the objectives of our epidemiologic studies of health and mortality among DOE workers included under the Oak Ridge project and on the role of the University of North Carolina in these studies. Our studies are addressing three research questions which constitute our main study objectives:

1. Is there any mortality excess among DOE workers?
2. Do DOE workers have more cancer than predicted, based on current radiation dose-response models?
3. Are certain DOE jobs or work environments, particularly those having exposure to higher levels of occupational chemicals, at increased risks of death from cancer?

I propose to discuss the significance of these research objectives, mention some of the problems we encounter in trying to answer these questions, and suggest some ways in which needed epidemiologic research on occupational hazards in DOE facilities could be facilitated.

A. Is there any mortality excess among DOE workers?

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Typically, working populations have SMRs significantly less than one because, on the average, people who enter the workforce have better health and experience lower mortality up to age 65 years than does the general population. This is so because the general population includes a significant proportion of disabled, unemployed or otherwise unemployable people whose life expectancy is well below average; this phenomenon is called the "healthy worker effect".

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B. Do DOE workers have more cancer than predicted, based on current radiation dose response models?

As you are aware, the controversial study of DOE workers at the Hanford, Washington facility by Mancuso, Stewart and Kneale (Reference 1) drew the conclusion that occupational exposure to ionizing radiation produced considerably more cancer than expected from the amount of radiation to which the workers were exposed. When other investigators (References 2,3) reanalyzed the Hanford data, they failed to confirm a number of the positive associations between cancer and radiation exposure, but they did confirm that an excess of multiple myeloma and cancer of the pancreas occurred. Studies of Hanford workers consistently failed to find any increase in leukemia mortality in spite of the fact that high dose radiation exposures regularly caused leukemia excess.

This finding demonstrates the importance of not relying solely on high dose radiation studies to evaluate risks at occupational dose levels. The finding of the myeloma and pancreatic cancer excess suggests either that the risk for these cancers is greater per unit of radiation exposure than predicted by other population studies, (particularly those based on much higher radiation doses) or that other factors such as chemical exposures may account for the observed excess mortality, or that the play of chance was not effectively ruled out. To evaluate these alternatives it was very important to study cancer mortality in other DOE facilities, especially those in which a sizeable population of 20,000 or more workers could be followed retrospectively. The Oak Ridge facilities are ideal for this purpose since they have a cumulative workforce of more than 100,000 workers and radiation dosimetry is generally excellent for this workforce.

What can we expect to conclude from the Oak Ridge studies with regard to cancer risk among DOE workers exposed to ionizing radiation? To answer this, we must know something about the distribution of cumulative radiation exposure among the Oak Ridge workers. The greater the number of workers exposed to higher levels of radiation, say near 3-4 rem per year (less than the annual occupational limit of 5 rem), the better the statistical probability of detecting an effect of radiation on cancer risk at occupational levels of exposure. Unfortunately for our studies, but to the credit of the radiation hygiene program at Oak Ridge, only a small proportion, about 10 percent, of workers had cumulative occupational radiation (whole body) exposures exceeding one rem as monitored by the radiation dosimetry program. For only 2 1/2 percent of workers did total exposures exceed 5 rems. Thus even among 100,000 workers we will find only 2500 with external radiation exposures more than 5 rem in their occupational lifetime. At these low levels of exposure, we cannot expect to detect any cancer excess that is less than 10 times that expected based on current dose-response models. However, in the light of the first Mancuso study of the Hanford workers, it is important for us to be able to conclude 1) whether there is any cancer excess, 2) whether this excess is as large as 10 times or 15 times the amount of cancer expected for the measured radiation exposure. That is, we need to state what the upper bounds of a confidence limit are for any estimate of cancer risk derived from our studies.

We will not be able to detect a radiation-induced cancer risk if this risk is less than 10 times expected. To do so we would have to study a significantly larger group of radiation-exposed workers, or we would have to find a group exposed to more radiation. But we should be willing to take one step at a time, and an important first step is to know whether any cancer mortality excess exists in this DOE facility and, if so, if there is any significant statistical relationship between amount of radiation and cancer risk. The upper bound of our cancer-radiation estimate will allow us to refute or affirm the apparently excessive claims of those who say that radiation cause 100 or 1000 times more effect at low doses than models predict. These questions we can answer.

C. Are certain DOE jobs or work environments, particularly those having exposure to higher levels of occupational chemicals, at increased risk of death from cancer?

This question is the most difficult of the three to answer satisfactorily. To do so, we must characterize not only radiation but also chemical exposures of the workers at Oak Ridge. Unlike radiation, chemical exposures are not monitored routinely, the number of chemicals utilized in many industrial processes is large, and exposure to chemicals cannot be simply reduced to a common unit of measurement. However, the health assessment of chemical hazards to DOE workers is extremely important. Many chemicals used in the nuclear fuel cycle have greater potential for toxicity and carcinogenicity than could be expected from ionizing radiation at occupational limits of exposure. The enrichment and processing of nuclear materials requires the use of these chemicals, and therefore we should be at least as concerned about the exposure of workers to chemicals as to radiation at DOE facilities. On an *a priori* basis, it would be reasonable to expect more cancer and other adverse health effects among DOE workers attributable to chemicals than to radiation.

The epidemiologic approach to the evaluation of chemical hazards in industry has developed considerably over the past 10 years. Our occupational epidemiology research group at the University of North Carolina gained considerable experience in this evaluation through an 11 year research contract negotiated by the labor union with the management of several large rubber tire manufacturing companies.

As a first step, one that does not require characterizing the chemical exposure of every worker, we divide the workers in a facility into functional groups based on the particular industrial process or simply on the department in which a worker was usually employed. Age-adjusted mortality rates are then calculated for each functional group or department and compared with the average rate for the entire facility. These results often give clues that certain work environments may be associated with increased mortality risks. The next step is to select chemicals or groups of chemicals that are known to be toxic or potentially carcinogenic and assign an exposure rank to each job for each selected chemical. This is a complicated, technical evaluation that requires input from industrial hygienists and job supervisors who are very familiar with the industrial process at the facility. The end result is a cumulative chemically-specific exposure index for each worker based on his/her entire job history. The mortality experience of workers on the high end of the exposure index can then be compared with those on the low end, or, a case-control study can be performed in which the cumulative exposure index of all persons dying of a specific disease, say lung cancer, is compared with persons not dying of this disease but matched with cases on age, age at hire and year of hire. These analyses begin to pinpoint whether there are particularly hazardous chemical environments within a facility and suggest what chemicals or groups of chemicals may be responsible for the hazard. They take into account the fact that a worker may change job assignments 10 or 12 times and may be exposed to different combinations of chemicals in each job.

To evaluate these complex chemical environments by relying on animal models would be prohibitively costly and infeasible in practice. The epidemiologic approach is the only proven method for detecting chemical occupational health hazards as they typically occur in an industrial environment. Thus, although several scientific bodies (References 4,5) have suggested careful limitation and selection of epidemiologic studies involving low levels of ionizing radiation (because of statistical requirements for very large study populations), this limitation should not apply to the broader occupational health assessment of groups involved in the nuclear fuel cycle, since we know exceedingly little about the health and mortality risks of the total occupational environment, chemical as well as radiological in the nuclear industry. Epidemiologic studies of DOE occupational health risks, particularly risks due to chemicals, deserve a high priority precisely because hazardous chemical exposures, when identified, can often be controlled by economical industrial hygiene measures.

D. The role of the University of North Carolina

Oak Ridge Associated Universities (ORAU) is a prime contractor to the Department of Energy and is the principal research unit responsible for the Oak Ridge health and mortality studies. ORAU is not one of the Oak Ridge facilities that are the object of our epidemiologic study, and it is desirable to have a prime contractor external to the study site. However, being a Department of Energy research laboratory, ORAU has more direct access to DOE data, computers and personnel than would be the case if a university were prime contractor. Our role, that of the University of North Carolina (UNC), is, in the main, twofold: 1) to bring added scientific credibility to the results of this overall project and 2) to provide the intellectual stimulus that is added to a project by involving doctoral students, their doctoral committee faculty, and the faculty researchers themselves.

Concerning scientific credibility, I do not believe that federal agencies or DOE laboratories lack scientific credibility, but there are critics of government research who claim that bias inevitably creeps into a study when the government studies itself or the consequence of its activities. Such bias is not, of course, peculiar to governmental activity and, in reality, the government research unit has nothing to gain and much to lose if it produces a biased negative evaluation. However the expectation of the charge of bias was good reason for ORAU to seek collaboration with a non-governmental research unit. I wish to assure this Committee that we are given ample opportunity to review and critique all of the work that results from this project. In carrying out our review function, we are not acting as external advisors to the ORAU research staff but as collaborators in the earliest design phases through data analysis and writing of reports. The exchange of ideas and personnel has been continuous and substantive. Some of our graduates are now employed by ORAU in the epidemiologic project, and some of ORAU's scientific staff have become students in our School of Public Health. Our research staffs meet once monthly for a full day to review protocols and progress and share research ideas.

Having doctoral students involved in a research project brings not only cheap labor but highly motivated, trained individuals who stay abreast of the most current scientific literature and are willing to try new research methods. Aside from this intellectual stimulus, the very fact that two organizations collaborate on a study ensures a degree of scientific review and challenge of ideas that might not be found in one group of longstanding peers.

A question that may be foremost to this Committee is: should the health and mortality study of DOE facilities continue as presently structured? In my opinion, biased as it is, the answer is a strong affirmative, not for social or political reasons (to answer those who claim much greater risks of radiation-induced mortality than present dose-response models indicate) but for the scientific and public health objectives related to the chemical and overall occupational health concerns for workers in the nuclear industry. As I have argued, compared with our knowledge of radiation health effects, we know relatively little about the health consequences of exposure to most occupational chemicals, and exposure to these chemicals is an inherent part of employment in the nuclear industry.

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Mr. GORE. Thank you very much.

I would like to thank all three of the witnesses on this panel for excellent testimony.

Can you briefly summarize, Dr. Shy, the portion of your statement that you skipped over in the interest of time on the effect on DOE workers?

Dr. SHY. On whether or not radiation effects——

Mr. GORE. I don't want you to read it——

Dr. SHY. What I said in there briefly is we would not be able to observe whether or not there is an effect unless that effect is 10 times more than that which we would currently predict from those responsibilities.

So, basically all we can do is say there is an upper limit to the amount of cancer that is being produced by radiation. That upper limit is either 10 times or more than would be predicted.

We cannot say the radiation effect is two times as great as would be predicted. The sample size isn't large enough and the exposure to radiation is simply not large enough to detect these small effects. I think it is important to put an upper bound on that estimate.

Mr. GORE. Dr. Thiessen, you say "After 32 years of medical followup, no evidence to date suggest that adverse health effects have resulted," et cetera. How confident are you about that statement and the data behind it?

Dr. THIESSEN. I believe that refers to the medical followup on the 26 Manhattan district workers. I think we are as confident as we can be on a medical practice level. Of course, a population of that size doesn't really allow any conclusions of an epidemiologic nature. If I were one of those 26 people, I think I would feel pretty good about it.

Mr. GORE. Do you have any improvements in coordinating Federal health and safety research efforts?

Dr. THIESSEN. As you well know, Mr. Chairman, we do have an Interagency Radiation Research Committee, which works very well. As a matter of fact, I have not heard any negative comments from any of the members or their staffs, and I would definitely be in favor of continuing the efforts.

Mr. GORE. But are there any changes or improvements you would recommend?

Dr. THIESSEN. I believe there are continuing discussions with respect to the establishment of new radiation standards, or a change in existing standards. I think such matters of policy with respect to radiation protection need to be discussed on a level that exceeds that of the Interagency Radiation Research Committee. The Radiation Policy Council, that existed until a few months ago, could have filled a very important gap. I would be in favor of its reestablishment.

Mr. GORE. You seem in some respects to be hedging your bet with regard to the usefulness of the ORAU study. Am I reading your testimony wrong?

Dr. THIESSEN. Well, the answer is yes. I do believe that if you interpret my comments as such, you are wrong. I am very much in favor of the study. Being an occupational health physician myself, I do consider this an occupational health study, surveillance of a worker population with respect to the evaluation and analysis for potential health effects related to occupational exposures. As such, I have the highest regard for it.

If I am critical, it is that I do not believe that the study will result in clear-cut, straightforward results with respect to the effects of low-level radiation exposure, but I am certainly not critical with respect to the objectives of the study.

Mr. GORE. Now, the FRIER report and the National Research Council's review of DOE research on human health effects of low doses of ionizing radiation both recommended a national uniform scientific peer review process for DOE should be developed. Have you taken any steps to implement this recommendation?

Dr. THIESSEN. The FRIER report repeated the recommendation of the earlier National Academy of Sciences review. Do realize, please, the earlier committee analyzed 16 projects in the human health effects area, out of more than 1,000 scientific projects that we have in the Office of Health and Environmental Research.

We simply do not believe that the recommendation of the National Academy with respect to an advisory committee was based on an adequate evaluation of our entire research program. However, as I said, we are not against an advisory committee. We do not believe, though, that it will impact on the peer review process as much as one may be made to believe.

Mr. GORE. Do you really consider conference with your peers to be a peer review?

Dr. THIESSEN. Absolutely, Mr. Chairman. Absolutely, no question about it.

Mr. GORE. What kind of peer review occurs before the contract is signed?

Dr. THIESSEN. If we have a proposal for an epidemiologic study our staff epidemiologist evaluates which outside reviewers should see it and he will determine two to four people to which the proposal will be sent. They will be asked for their opinion.

When these come back, there is an internal review among our own staff. Then the proposal is brought before the research committee, which is basically a conglomerate of all of the professional staff of the Office of Health and Environmental Research. Then a recommendation is made to the Director of the Office as to whether or not the proposal should be supported.

Mr. GORE. You mentioned site visits. Do you personally review the recommendations?

Dr. THIESSEN. Yes, sir.

Mr. GORE. Are they implemented?

Dr. THIESSEN. If we agree to them, yes, sir.

Mr. GORE. How long do you expect the health and mortality study to continue?

Dr. THIESSEN. As long as there are worker populations for which the department has a responsibility, the study will continue.

Mr. GORE. Is there some plateau that will be reached when conclusions are framed?

Dr. THIESSEN. No, I think what will happen, Mr. Chairman, is that the biological end points may change. Maybe not so much with respect to the radiation exposure, because I think all indications are that the level of radiation exposure will go down in the future; if anything, but there may be other occupational hazards that appear on the horizon. I think that will result in new biological end points to be studied. So the character of the study may change, but I don't think it will, as you call it, level off.

Mr. GORE. Does it have then no logical conclusion?

Dr. THIESSEN. The conclusion with respect to what?

Mr. GORE. With respect to the effects of what it can tell us about the effects of low-level ionized radiation.

Dr. THIESSEN. If you want to discuss low-level radiation, as I explained, I don't think that we will ever have a definitive answer to the question of what are the exact effects of low-level radiation.

With respect to the boundary conditions that Dr. Shy discussed, yes, we can set boundary conditions and probably say within a number of years—frankly, I could not give you an exact number of years—we will have met the requirements and will have demonstrated, for example, that the effects are not worse and cannot be as bad as whatever boundary condition we set.

Frankly, I do believe that the emphasis on low-level radiation is not entirely justified. I think there are other occupational hazards in the DOE worker population, and they are as much a part of the study as the low-level radiation exposure.

Mr. GORE. Did you say that the primary objective is not to determine the health effects of low levels of ionizing radiation? That is not the primary objective?

Dr. THIESSEN. There are much better ways of doing that. You have to realize we have to take human populations as they are. We can select animal populations, but cannot do that in humans.

Mr. GORE. What is the objective of the study?

Dr. THIESSEN. The objective of the study from the point of view of low-level radiation exposure is to determine whether radiation effects related to low-level exposure are much more serious than predictable on the basis of extrapolation from high dose data.

Mr. GORE. When do you think you will reach a conclusion with respect to that question?

Dr. THIESSEN. I think we have reached a number of conclusions already. I think it is pretty clear from all we know today that those effects are not much worse than those predicted from the existing data base.

Mr. GORE. So you have already reached the conclusion that you expect is the primary objective?

Dr. THIESSEN. I don't think we have evaluated enough of the DOE population.

Mr. GORE. When do you think you will?

Dr. THIESSEN. We have to go back in the past. The Manhattan Engineer District workers, of course, far exceed the number of people we presently employ.

Frankly, I hate to give you a date because that is very much dependent on the work program that Dr. Lushbaugh is carrying out. I would be very surprised if we see a severe cutback in the level of support, for example, for the study within 10 years. That is a very rough estimate, but I wouldn't expect that the extent of the study will go down any within that period.

Mr. GORE. What are the present funding levels for the health and mortality study?

Dr. THIESSEN. In fiscal year 1982, $3.3 million.

Mr. GORE. That is the total in the category, if I am not mistaken?

Dr. THIESSEN. Yes.

Mr. GORE. Dr. Lushbaugh, you may have these figures at the tip of your tongue?

Dr. THIESSEN. A little more than $2 million.

Dr. LUSHBAUGH. That is the number I have in my head.

Mr. GORE. Is that figure expected to increase?

Dr. LUSHBAUGH. Hopefully.

Dr. THIESSEN. You bring up a tender point, sir. Of course, if you ask how long the study is going to last, it is very much related to the level of support. Dr. Lushbaugh can only do so much. If you double his staff, and we have to go back in history as I explained, he can do the whole work on the population faster than he does now.

Mr. GORE. The design of the study ought to have some end point built into it, shouldn't it?

Dr. THIESSEN. The reality is that we are subject to budgetary limitations related to the entire program of the President.

Mr. GORE. To what extent are you seeking merely to discharge the responsibility?

Dr. THIESSEN. I think it is an important one. In my view, the major consideration why we do the study and why we continue doing it.

Mr. GORE. That goal takes precedence over the goal of determining?

Dr. THIESSEN. I think it could in time, but we are talking about basically different things.

Mr. GORE. Dr. Lushbaugh, let me ask some of the same questions of you. How long do you think this study will continue or should continue?

Dr. LUSHBAUGH. Well, I think that we are within 1 or 2 years of having some very definitive results to be able to show you and we believe at that time we will be able to begin to merge some of these small study segments into larger ones and that I, myself, in the plan that I have in my head can see that in 6 to 8 years we would have analytical files and data bases so developed that you would have the national resource for epidemiologists to attack all sorts of problems with its use and that I think that the difficulty with your question is that as one explores these data and finds these answers they raise other questions that are of great national interest.

For instance, we see in many of the studies which we are doing which are in preliminary phases that there is a very significant trend in these workers for cancer of the lung.

Now, these workers are carrying that trend all over the United States. Now, whether or not that is just cigarette smoking or what else it is we don't know but there is no other data base that I know of available or being prepared in the United States which is comparable to the huge size of this one that we are putting together.

So the short answer is I would think you would have quite credible answers to many of the questions in 6 to 8 years but in getting those answers I think you are going to create more questions which will generate more studies which will keep it going on. But they will be different studies.

Mr. GORE. Now, the reviewers in 1980 and 1981 characterize the work as heavily concentrated in surveillance activities.

Is the emphasis of the health and mortality study on surveillance or its emphasis on the development of new knowledge of health hazards associated with employment in the nuclear industry?

Dr. LUSHBAUGH. Well, I don't agree that it is heavily concentrated on surveillance.

Mr. GORE. They did say that, though?

Dr. LUSHBAUGH. They did say that, yes.

I think that they derived that from some of us excusing our lack of results in regard to the radiation effects and saying that, even so, these studies were important because of their ability to provide DOE with surveillance of the nature of their safety programs for other chemical and other metallic hazards.

So I would like to rewrite what they said but I don't always have that opportunity.

Mr. GORE. I don't either. I had a similar experience.

Just to go on with the reviewers comments, they also stated that, "Each study seemed to stand alone," and each was viewed "as constituting a unique exposure situation with little, if any, possibility of relation to any overall evaluation of occupational hazard."

I would like you to comment on that and then ask you whether anything has been done to bring together this group of projects for a coordinated interpretation of the health hazard?

Dr. LUSHBAUGH. I think time is answering that question. I think at the time the committee reviewed our program and saw what was happening they were justified in saying that they saw it as many small projects. They didn't see it from my management point of view, though, where if you will recall my one viewgraph showed the study process.

Phases 1 and 2 at one laboratory could be quite far ahead and then suddenly because of some management problem would grind to a stop and some other study would come along and go up to an analytical file and be analyzed.

A student who wishes to finish up his Ph. D. suddenly, for some reason or another, will seize upon a small project that we need done sometime.

This offers an opportunity to get this one little part done which I see in the overall view to be needed sometime, although not particularly then but the review committee sees these various fragments getting done at different times.

But because the whole process takes up to 6 years you can't study these various plants and plant process is consecutively one after another.

They have to be done concurrently and as concurrently as you can do them making use of staff that is not involved in one study because it stopped.

Mr. GORE. Well, now they also recommended an overall study plan. You feel that you have implemented that recommendation?

Dr. LUSHBAUGH. I believe we have. And I think that with our review process with the University of North Carolina we now have in place a large plan which I believe is going to produce the results that the committee would be proud of.

Mr. GORE. Dr. Shy, do you want to respond to that question also?

Dr. SHY. Yes, I think that as we become more familiar with different study populations available to us, an integrating element begins to appear. In other words, we are seeing workers who were involved in the early phases of the nuclear industry where exposures were considerably higher than they are now.

We are seeing workers who are processing uranium. Workers who are involved in later stages of the nuclear cycle, enrichment of uranium and then scientific radioisotopes, so we are seeing workers exposed to different phases of the nuclear fuel cycle at different time periods when there was high exposure versus present times where exposure is much more carefully controlled, I believe.

All of those tie together to give us evidence of different dose levels and different types of exposures, uranium as a chemical and uranium as a radioactive compound and ionizing radiation only as an external form of exposure to humans.

Putting that all together the picture begins to emerge of where the health hazard lies and perhaps what does emerge might be associated with greater risks.

Mr. GORE. Now, you stated, Dr. Shy, that unlike radiation, chemical exposures are not monitored routinely, yet the health assessment of chemical hazards of DOE workers was extremely important, particularly since the toxicity of some chemicals used in the fuel cycle has greater potential for toxicity and carcinogenicity than low levels of ionizing radiation.

What steps have been taken to assess chemical hazards?

Dr. SHY. The steps we are taking is to be able to identify the job title of a worker as he progresses through his work life and relate that job title to the chemicals to which he was exposed.

So we have to convert a name like a job title into some kind of quantitative estimate of what exposure he might have had to solvents, to the uranium, to fluorides, to any other compound that might be of concern.

The only way we can do that is by becoming familiar with the process in the industry.

Mr. GORE. The National Research Council concluded in the 1980 review that the populations used are too small to permit derivation of statistically significant information and conclusions if the effects are about the same as expected on the basis of previous studies.

Could you comment on that conclusion?

Dr. SHY. That was radiation they are talking about. Yes, I mentioned that in my testimony that we could probably only detect as statistically significant cancer mortality if that mortality is 10 times greater than the classical knowledge would predict.

If it is near the level that they would predict we would not be able to detect any excess and that is the whole argument about doing epidemiological studies of lower level ionizing radiation.

It is unlikely that we will be able to observe directly an effect if effects are as low as predicted. However, we do need to answer the charge of some people saying that effects are 10 to 100 times greater than the classical models predict. If they are that great we will be able to see them.

Mr. GORE. I see. But if it is only eight or nine times greater——

Dr. SHY. We may not be able to see them. The only way you can see effects at that level is to have more people or to have higher exposures of the limited number that you have.

As it turns out there is very little radiation exposure among DOE workers.

Mr. GORE. Let me go back to the chemical exposures for just a moment. You said you were going to isolate that variable by looking at job titles.

Are you satisfied that that is an adequate way to do that? How can you do that?

Dr. SHY. It is not a perfect way to do it. A better way would be to have direct measurements of the chemical exposures that individuals were being exposed to but there are such direct measurements but nobody had instrumented monitors to measure these.

We have to use these indirect or surrogate measures of exposure. The job title is a very good surrogate of exosure because it is an accurate history of what the worker was doing on the average at least for virtually every day of his working life.

So you can convert that job title into a chemical exposure index. By an index I mean that you don't get, necessarily, a unit of, say, 10 units, 5 units, but what we can estimate is whether he had no contact, some contact or potentially quite severe, quite extensive contact with a given chemical.

Mr. GORE. Back to radiation now. Let's suppose that the study shows a strong effect. Does that constitute evidence that the exposure data is inaccurate?

Dr. SHY. Not necessarily. I think the exposure data externally is very good. If we found very severe effects, I guess we would have to say that, No. 1, either radiation is producing much worse effect than we thought, or; No. 2, there are chemicals involved here that are producing the effects.

We have ample ways, though, to discriminate between radiation and chemicals for the most part. So we should be able to answer the question.

If there is an excess effect can we say that it is more likely due to radiation or to chemicals? I think we can handle that.

Mr. GORE. Well, how can the available chemistry data be used to segregate populations into different risk groups?

Dr. SHY. Well, each worker has a cumulative radiation dose measuring his total occupational lifetime exposure. With that dose you can categorize people as to those you say have had more than 5 rems over their lifetime and those who have had 5 to 5 rems and those who have had less than that.

Mr. GORE. And you think that data is pretty good?

Dr. SHY. I think that data is generally quite good. Now, there are some problems in that internal radiation exposures are not monitored by that device. So if you inhale a particle that is radioactive you don't measure it with a radiation badge.

Mr. GORE. Let me ask you about the computer system. Some of the viewers expressed concern about the data management and they noted that the present DEC-10 has a limitation and it can't address more than 256,000 individual records in a given subfile.

It is my understanding that some of the data bases currently being stored on IBM systems and that this data is selectively reloaded the DEC-10 system on a demand basis; is that correct?

Dr. SHY. Let me pass that question to Dr. Lushbaugh.

Dr. LUSHBAUGH. Yes, I think that is my department.

The way this operates at the present time in the Oak Ridge system that we have, we have 2 PDP-10 systems back-to-back and we use a data management system called 1022 and the company that is responsible for this software is in the process, and has been in the process, of constantly improving the 1022 management system.

At the present time we can only have 11 open files from which we are feeding on when we are running in actual contact with the computer but this is a mass of data that is so much larger, interactively, than anybody else is doing today that Dr. O'Kane's comment is really facing what he thinks we ought to be doing 5 or 6 years from now, and he is criticizing us for not somehow or another modifying our data management system when no other better system exists.

It isn't true that we are storing data on an IBM system. We are actually using the IBM system with the 3033 and the SAS management system because our various kinds of models work better on that system as an analytical system than they do on the PDP-10.

So it is a Tower of Babel type of thing.

Mr. GORE. Have there been any problems in transferring the data to North Carolina?

Dr. LUSHBAUGH. No, we encrypt all our data for privacy reasons and use these employment identifiers, which only we know who they are and where they worked. This is an encoding system that protects them under the Privacy Act.

And the problems that they foresee, or they did foresee, is in some of these smaller data sets in the transportation of disks and data packs and the like with automobiles and the like, that it wa essentially time-consuming but it hasn't worked out that way.

Mr. GORE. Fine.

We have so many other witnesses I am going to cut this short and perhaps if you would be willing to respond to additional questions for the record, I don't anticipate too many of them but if you would, we would appreciate it very much.

Thank you very much for coming here today and helping us in our inquiry.

I would like to now call our second panel. Dr. George B. Hutchison with the Harvard School of Public Health; Dr. Gilbert W. Beebe with the Clinical Epidemiology Branch of the National Cancer Institute of MNIH, and Seymour Jablon, director of the medical followup agency at the National Research Council.

Gentlemen, if you would come forward and raise your right hand, please.

[Witnesses sworn.]

Mr. GORE. Without objection, the entire text of your prepared statements will be put in the record in full and we would like to invite you to proceed with either a summary or all of it as you see fit.

We really appreciate your willingness to help us in this inquiry into a difficult subject and we would like to begin, Dr. Hutchison, with you. I would like to welcome you and invite you to proceed.

STATEMENT OF DR. GEORGE B. HUTCHISON, HARVARD SCHOOL OF PUBLIC HEALTH, DR. GILBERT W. BEEBE, CLINICAL EPIDEMIOLOGY BRANCH, NATIONAL CANCER INSTITUTE, NATIONAL INSTITUTES OF HEALTH; AND DR. SEYMOUR JABLON, DIRECTOR, MEDICAL FOLLOW-UP AGENCY, NATIONAL RESEARCH COUNCIL

Dr. HUTCHISON. Thank you, Mr. Chairman. My name is George B. Hutchison. I am a physician and employed by Harvard University as a professor of epidemiology.

I have been a member of the Advisory Committee to the Medical and Health Services Division at Oak Ridge for approximately 4 years.

I have been engaged in research in human health effects of ionizing radiation for 20 years.

The health and mortality study which is now being carried out at Oak Ridge University involves the long-term investigation of employees of the Department of Energy and of contractors to the Department of Energy with special reference to possible health hazards of this employment, including exposure to ionizing radiation, toxic metals, and industrial chemicals associated with nuclear technologies.

These studies were initially undertaken under Government contract at the University of Pittsburgh and with a more limited focus on effect of ionizing radiation and on a limited group of employees.

At the time of initiation, completed studies of effects of ionizing radiation in human populations were very limited, and estimates of doses received in most industrial settings and of effects of such exposure were similarly limited.

In particular, it was known that in the occupational setting of hard rock mines and especially mines with a substantial content of radioactive metal workers were exposed to very substantial radiation doses and were in consequence subject to a large hazard of radiation carcinogenesis, particularly from lung cancer.

Little similar information was available about other occupational settings in which there was known or presumed radiation exposure. Permissible levels of occupational exposure to radiation had been established.

It was not well-known how frequently and to what extent these levels were exceeded in actual practice, nor to what extent individual workers accumulated permissible or near permissible levels repeatedly over many years, nor what health effects were expected from permissible exposures and from greater exposures in actual practice.

In the face of the above uncertainty it seemed to many scientists highly desirable to obtain initial data on exposure and outcome.

Such questions were posed largely as descriptive studies with limited guidance from any quantitative predictions which might be expressed as specific hypotheses.

In the years since 1965, a very extensive literature on health hazards to human populations exposed to ionizing radiation has developed. This includes information on populations exposed to radiation used in military operations, maneuvers, and weapons tests, and populations exposed to a number of occupational uses of ionizing radiation.

Effects in the nature of cancer induction have been most prominent, have been demonstrated for a large number of cancer sites and histologic types, and have been expressed in quantitative terms in association with radiation doses in the range of 100 rads or greater.

In these high dose ranges both human population studies and experimental studies in a number of biologic systems have allowed the quantitative estimation of carcinogenic effects.

A number of comprehensive reviews of this growing body of data have been prepared by the National Academy of Sciences in the United States and by the United Nations Scientific Committee on the Effects of Atomic Radiation.

Over the same years uniform reporting systems for exposure to ionizing radiation have been increasingly employed in occupational settings and data on these exposures have been assembled for very large numbers of employed persons.

Quantitative statements can now be made both about the health hazards of high dose radiation exposure, over an extensive high dose range, and about the distribution of employed persons with respect to occupationally incurred radiation exposure.

One striking result of this accumulated information is that the two bodies of information, exposure and hazard, are poorly coordinated.

The exposures are distributed in the 1 rad range (0.1 to 10 rad), an order of 10 above or below 1 rad. And we saw some distributions of that a short while ago.

Hazard estimates are reasonably reliable chiefly in the range of 100 rad and higher.

In recent years numerous attempts have been made to reconcile the exposure and the hazard data. Mathematical reconciliation is attempted by interpolating between the known high dose effects and the logical presumption of zero effect at zero dose.

The proper method of making this interpolation may be inferred in part from experimental data in nonhuman biologic systems, but even there a limitation exists in the low dose range, where effects are rare.

All such interpolation involves substantial uncertainty. Direct observational reconciliation has been attempted by a limited number of epidemiologic studies, chiefly in the past 5 years, in populations exposed to low doses. The present health and mortality study is among this group of low dose studies.

With regard to study design, the present study differs from the initial study plan in several important ways.

First, the initial study was designed as an observational study in an area where reliable quantitative knowledge was sparse. There is extensive knowledge now available. Remaining unanswered questions are in an area where the ability of scientific investigation may be limited by practical constraints.

Second, the initial study was directed at a rather limited and clearly finite population. The present study design is related to a vastly larger population already accumulated, approximately 600,000 employees, and to an open-ended time period of new employee accrual and of continued followup of present employees.

An epidemiologic scientific study design is ordinarily related to specific quantitative hypotheses when a basis for formulating such hypotheses exists.

Furthermore, the design includes considerations of statistical power, or the probability of confirming the hypothesis if the hypothesis is correct.

For sound scientific reasons it is widely felt that study designs are deficient if they involve poor statistical power, that is, if the associations to be studied are believed to be so weak that a study of feasible size may fail to recognize the association.

In the present instance there exists some controversy as to what the present best hypothesis is.

Some scientists feel that the body of present information on effects of radiation is sufficient to lead to a conclusion that the effect of radiation doses experienced by any large proportion of Department of Energy employees is so small as to imply deficient statistical power for any epidemiologic study of this effect.

Some other scientists reach a substantially different evaluation of present knowledge and judge the risk to be very much larger, hence, giving good statistical power in terms of these larger risk hypotheses to the present study design.

In addition to the consideration of statistical power, there is a consideration of a practical limitation on epidemiologic studies.

If power alone were at issue, one might contemplate simply extending such a study to arbitrarily large populations followed for arbitrarily long times.

The required population size can be determined mathematically for any prior assumption as to the best hypothesis, and provided the resulting number does not exhaust all available populations that power could be achieved.

Such a study, however, could not in fact be carried out. The limitation is that of control of confounding.

In an observational study it is generally felt by epidemiologists that if an association is in nature weak, as, for example, when the excess risk association with a small radiation dose is only about half, or less, of the natural or spontaneous risk of the same cancer, then it is impossible to gain any confident assurance that an association is causal.

The alternative interpretation is that any of a number of other small hazards may be equally likely explanations.

Note that this is a limitation posed by the true biologic relation of small effect at small dose, and is not overcome by large numbers of study subjects. No numbers would suffice.

Finally, the open-ended study design, involving both present and future employees for indefinite time, argues against a scientific study. Such an open design suggests a surveillance operation rather than a scientific study.

Let me comment, then, on surveillance studies.

The advisory group, of which I am a member, has tended to adopt the position that the present study is a surveillance operation.

We have attempted to evaluate the ability of the present operating group to conduct comprehensive surveillance of the employee populations.

As a surveillance operation I have been pleased with the working team assembled by Dr. Lushbaugh. Members of this advisory group qualified in statistics and in computer science are similarly impressed with this working group.

Members concerned with toxicology, including study of chemical and heavy metal industrial exposure, have made important suggestions for better evaluation of these areas.

In general, however, the surveillance operation is judged to be of good quality and is perhaps unique in terms of the scope, including so large and diverse an employee population.

Mr. GORE. Doctor, let me stop you there. I apologize. We have a vote and it will be a very brief recess.

[Brief recess.]

Mr. GORE. The subcommittee will come back to order. Sorry for the length of these proceedings, gentlemen. Dr. Hutchison, please proceed.

Dr. HUTCHISON. I would like to mention next what I see as some of the principal and outstanding issues in connection with the comments I have just made.

No. 1, is the hazard of low dose ionizing radiation sufficiently well-known to determine the statistical power of these studies?

No. 2, is the present work a scientific study or a surveillance operation?

No. 3, if this study is viewed as a scientific study, is it properly designed to answer the appropriate scientific questions?

And, finally, if it is viewed as surveillance, is it properly designed for surveillance?

The question of the present state of knowledge regarding the hazard of low dose radiation has been reviewed by several authoritative bodies in recent years.

Two such reports by committees of the National Academy of Sciences are:

"The Effects on Populations of Exposure to Low Levels of Ionizing Radiation: 1980, the BEIR Report," and "Federal Research on the Biological and Health Effects of Ionizing Radiation, 1981," that has been alluded to this afternoon.

In both of these reports and in all other reports of authoritative bodies of scientists there has been agreement on certain aspects of radiation hazard. In particular, it is generally agreed that estimates of cancer risk at doses in the range of 100 to 300 rad are sound.

It is found that in these ranges risks increase regularly with dose but that at the upper end of this range or somewhat higher there may be an absolute reduction of cancer risk with further increasing dose.

It is generally agreed that cancer risks exist at doses below 100 rad and that these risks decrease with decreasing dose with either no threshold dose or with a threshold at a dose well below 100 rad and probably below 1 rad.

It is generally agreed that the nature of the decreasing risk with decreasing dose in the 10- to 100-rad range is approximately linear and that to the extent that it departs from linearity risks are somewhat lower than those estimated on the linearity basis.

There remain important uncertainties beyond the above agreed relations. In particular, there is poor agreement as to how great the deviation from linearity may be. There is poor agreement as to the nature of the decrease of risk with dose in the range of 0 to 10 rad.

It is to be noted that (1) these authoritative bodies do not disagree as to whether risk may be greater than that estimated on the linearity basis in the range of 10 rad to 100 rad; and, (2) they do not disagree on whether risk begins to decrease with increasing dose in the 10-to-100-rad range.

A small group of individual scientists do find disagreement with the positions of these authoritative bodies. In particular, some individual scientists interpret the evidence to imply a risk in the 10- to 100-rad range greater than that estimated on the linearity basis.

Some scientists interpret the evidence to imply a peak risk in the 0- to 100-rad range, followed by a lesser risk within this range.

With regard to the continuation of the present Department of Energy studies a determination should be made as to the credibility of interpretations of present evidence and particularly of the several major reports and the positions of certain dissenting scientists.

If the major reports are found credible, there remains in my mind no scientific basis for the Department of Energy studies broadly, though there may be certain specific scientific questions that may be usefully addressed within this body of data, as, for example, questions of certain industrial toxic substances, hazards of lifestyle characteristics such as smoking, alcohol consumption, and drug consumption, and hazards of traumatic accidents in these industries.

If, on the other hand, the dissenting views of individual scientists are found credible, the present studies may be found to be appropriately designed to address these questions.

With regard to surveillance, if this is the objective of these studies, that should be stated clearly.

A responsibility of major industries for surveillance of occupational health is widely accepted in the United States and other industrial countries. There is no generally accepted standard of procedures for such surveillance.

Persons with professional training in occupational health should become members of the surveillance group and should eventually accept a major role in setting standards for the particular surveillance plan for the Department of Energy.

Such surveillance should relate in appropriate balance to all hazards or potential hazards in these industries, whether associated with ionizing radiation, industrial toxic chemicals or heavy metals, or industrial traumatic accidents.

Questions of specific lifestyle habits of employees in this industry might or might not be deemed appropriate objects for surveillance.

Thank you, Mr. Chairman.

Mr. GORE. Thank you for a very excellent and useful statement. We will withhold questions until the other members of the panel have concluded.

Dr. Beebe, please proceed. We are delighted to have you.

Dr. BEEBE. Mr. Chairman, you have my statement. It perhaps is overlong to read. Let me simply try to summarize the main points. I should start with three caveats, however.

One, that I am appearing here as a private citizen, not as an employee of HHS or the National Cancer Institute.

And, second, that my personal experience in the area of radiation research was confined to studying the A-bomb survivors in Japan, which is a far simpler experience than what we are talking about today.

And, third, I am really no expert on the ORAU study. I am just learning how to pronounce it today but I have read the documents furnished to me and the papers that have appeared. It seems to me that the main thing I could do for you would be to provide a kind of independent opinion as to the scientific merit of this study.

I have organized my testimony around the questions listed for this discussion. The first one had to do with the value of the study scientifically. First I should say that although we think we know an awful lot about the human health effects of ionizing radiation there are some very large gaps in our knowledge, especially as to why risk estimates that we calculate vary as much as they do among different kinds of people in different situations and so on, and what the risks actually are at low levels, as has been stressed.

One of my concerns is that there not be too many low dose studies. I think that there is no real scientific need to show, yet, again, that ionizing radiation causes cancer. We know that.

So what I have done here on page 3 is to list some of the points that I think are appropriate scientific goals from an epidemiologic standpoint and I think perhaps two of them are most relevant to the discussion today.

One is that we don't really know what is the most appropriate mathematical form, or it may be forms, plural, for describing the relationship between human health effects and radiation doses.

And, second, whether and to what extent the effect of radiation is influenced by the rapidity with which the dose is delivered.

The A-bomb experience derives from an instantaneous dose. Here we are talking about doses that are received in dribbles.

Now, if we knew the best mathematical form for dose response, then I think we would know with considerable confidence how to estimate low dose risks. And we don't.

So, then, the alternative seems to be to attempt to estimate them directly. Unfortunately, in my opinion, these risks in the low dose region are so low that, as Dr. Hutchison has indicated, you just can't distinguish them from the inherent by variable biological experience of man, particularly in cancer.

Mr. GORE. Dr. Beebe, I would ask you to hold at that point and I apologize. Our committee has a series of close votes on the floor and we have another one now and it will be another short 7-minute recess, and I apologize to all of you. I know it is frustrating.

[Brief recess.]

Mr. GORE. The subcommittee will come back to order.

Again, a redundant apology. I think that we worked out a relay system for the next vote so we won't have to stop. Please go ahead.

Dr. BEEBE. I was talking about what I personally believe to be the near fruitlessness of the so-called low-dose studies. In my written testimony I indicated I had recently written an article on the A-bomb survivors. I was very pessimistic about that.

Studies of the A-bomb survivors are not going to solve the low-dose problem. For example, I give a couple numbers in there. Of the 82,000 survivors under study in the large mortality surveillance study, about 20,000 persons are exposed to 1 to 9 rads and another 14,000 exposed to 10 to 49 rads. These are very large samples in relation to anything that we have in the literature, but are not large enough to provide stable estimates of risk in the low-does range.

While the ORAU material that I have seen mentioned about 600,000 persons, I think that almost all of them have been exposed occupationally to less than a rad. The effective part of the sample seems to be the 5 rems a year group, and that is defined as at least 5 rems in at least 1 year, not 5 rems per year continually. We are not talking about people who got 50 rems, but people who got perhaps 15 or 20 rems. For many of them the total dose may be only 10 rems.

That sample includes only about 3,200 individuals. The Hanford study has 2,800 individuals exposed to 5 rems or more. So, intuitively and also with a little informal calculation I can't bring myself to believe that the ORAU studies can produce significant information on the risk in the low-dose region that we are most concerned about.

I would agree with what I have heard that the study may help to rule out a level of say 10 times conventional wisdom, and I am one of those who are in favor of 1 or 2 such studies.

I just don't want to see any more than one or two because I think the answer to the low-dose problem is not going to come this way. It is not going to come by trying to make a point estimate directly on the basis of an average exposure of 5 rads or 3 rads.

I think it will come through experimental and theoretical studies and through their interaction with epidemiological studies. Hopefully, epidemiologic studies will suggest some hypotheses and ideas for investigation and be used as the testing ground for whatever models the experimentalists and the theoreticians come up with.

Now, moving to the question of its general scientific significance in the field of ionizing radiation, I can't see any real chance that the ORAU study will come up with anything. There is a possibility that something might come from an interaction between a chemical exposure and radiation.

That seems to me an abstract possibility. The reason I say that I think nothing very important scientifically is likely to come out of it—one always hopes for serendipity in things like this—is that they will not have more than a handful of excess leukemias and maybe a score or two of other radiogenic cancer in the 5 rems study.

It is only when you have a relatively large excess—not 5 cases, but 50 or preferably 100 or more—that you can subdivide the material into groups or categories of people or of experience and from this begin to get answers that are of scientific interest.

One reason why the A bomb survivor study has been so productive is that there are about 90 excess cases of leukemia, we think, and about 160 excess deaths from other forms of cancer, in the study sample through 1978.

In addition to that, there are 40 excess incident cases of breast cancer. Even with the 40 cases of breast cancer, it has been possible to derive differential risks of scientific significance. In fact, they are rather exciting.

I would mention, without detailing the list here, that recently there have been a number of important warnings not to expect too much from low-dose studies. I cite them here on page 6.

So, from the scientific standpoint, I think it is studies of exposure to intermediate and high-dose levels that we need to do, studies that will generate enough cases to do something scientifically.

However, reading the ORAU material, I gained an impression that the exposure to agents other than ionizing radiation may be much more important than the exposure to ionizing radiation, I also can't help but feel that with the UNC group on board there are very likely to be important methodologic innovations.

I am sure that the UNC group is going to do something with their exposure to this large body of data, and that something will turn out to be very useful to all of us, even if it is only of methodologic significance.

Then, of course, as one who is interested in seeing the radiation epidemiology develop, I am very pleased to see that they are bringing students into it. I understand one of these students has chosen this as a basis for a career.

So, I say on page 7 that I regard the ORAU as a kind of defensive maneuver, a response to public and congressional pressure. I think it was politically and socially necessary that the study be redefined and reinstituted in 1977 or thereabouts. I regard it as a kind of insurance against the chance of conventional wisdom about low-dose risks being wrong by an order of magnitude.

I personally feel that such an outcome is very unlikely, but I recognize that many people have that worry. I also feel that when workers are exposed to known toxic agents, or to agents of unknown toxicity, they should be monitored for their health effects.

It seems to me that as a monitoring exercise alone, the study of these workers is terribly important. The optimal of design may not be exactly what ORAU and UNC have outlined but a study is important.

I move to the second question. I really can't help you there. I don't know how the outside consultants have interacted with investigators.

You also ask about the NIH Inter-Agency Radiation Research Committee and how it could be improved. I do point out that of course it is not an NIH committee: It is an interagency committee.

I hesitate to speak about it much because I have had very little experience with interagency committees, so that it is hard for me to compare the track record of this one with others. But subjectively, and from general experience, it seems to me it has accomplished a great deal.

I have listed some of the accomplishments and I will mention here only two: First, the Federal strategy for research into the biological effects of ionizing radiation; second, the FREIR report, which was commissioned by the IRRC and performed by the National Academy of Sciences.

I am impressed by the way people have come to IRRC meetings, by the leadership, and by the quality of what I have seen. I really have no suggestions as to how it could be improved.

As to your last point, the NASA review of the DOE study, I have read it and would tend to agree with what is said there, but I really don't know of any steps that may have been taken to carry out its recommendations. I am just not that close to the ORAU operations.

I will be glad to answer any questions.

[The prepared statement of Dr. Beebe follows:]

Statement by Gilbert W. Beebe, Ph.D.

Before the

Subcommittee on Investigations and Oversight

Committee on Science and Technology

U.S. House of Representatives

Wednesday, May 19, 1982

I am a medical statistician retired from the National Research Council where I was Director of the Medical Follow-up Agency, and am now serving as an expert at the National Cancer Institute. I am appearing at the invitation of the Subcommittee as a private citizen and not as a representative of the National Cancer Institute or the Department of Health and Human Services. A brief biography is attached but I should like to emphasize that my personal research experience in the field of ionizing radiation is confined to the health effects of radiation from the atomic bombs dropped on Hiroshima and Nagasaki in 1945. I have engaged actively in these studies since 1958, including six years spent in Hiroshima and Nagasaki. I should also make it clear that I have had little personal experience with the subject of today's hearing, the ORAU study of DOE workers, and am not an expert on that study. I have known of its existence for several years, have read the few papers published by the ORAU group as well as background material sent me ten days ago by the staff of the Subcommittee, and participated in the recent DOE Radiation Epidemiology Contractors' Workshop at which the DOE study was presented. Perhaps I can be most helpful to the Subcommittee in providing an independent opinion on the likely scientific yield of the project.

The outline for the hearing contains several questions that I will try to answer.

1) Value of DOE study on health effects of low level ionizing radiation on DOE workers?

(a) At what radiation levels are such studies more scientifically meaningful?

Although much is known about the health effects of ionizing radiation the gaps in our knowledge seem large, especially as to why risk estimates vary as they do, and what the risks are at very low levels, i.e., between background and the occupational limit of 5 rems per year, or perhaps 10 to 20 rems in a single dose. In my view, there is no scientific need for more demonstrations that ionizing radiation produces cancer; what we need are efforts aimed at gaps in our knowledge. We need to know:

(1) how the quality or the type of radiation modifies risk estimates;

(2) what is the most appropriate mathematical form, or forms, for describing the relationship between the effects and the doses that produce them;

(3) what host factors influence dose relationships, and in what way;

(4) whether there are other environmental hazards that interact with ionizing radiation to potentiate or even reduce the effect expected from radiation alone;

(5) whether or to what extent the effect of radiation is [illegible] the rapidity with which the dose is delivered to its target;

(6) how risk varies among target organs and tissues;

(7) whether there are important subsets of individuals in the general population with a very different level of sensitivity to the influence of ionizing radiation;

(8) how radiation-induced effects are distributed over time after exposure; and

(9) how to project risks into the future, beyond the period of observation.

If we knew the best mathematical form, or forms, for dose-response we would know how to estimate low-dose risks. I am one of those who believe that we cannot expect to estimate such risks directly, that they are too low to be disentangled from the inherently variable background levels of risk that we experience apart from any additional exposure to ionizing radiation. In one of my recent papers on the A-bomb survivors (Am J

Epidemiol 114:761-783, 1981) I have explained why I believe that studies of the A-bomb survivors, fruitful as they have been and will be for some years, will not solve the low-dose problem. And the sample of 82,000 survivors under study includes about 20,000 persons exposed to 1-9 rads (these are whole-body external doses) and another 14,000 exposed to 10-49 rads. These are very large samples in relation to other sources. Although the ORAU material includes numbers on the order of 600,000 persons the vast majority apparently received occupational doses below one rad; the 5 rems-a-year sample is said to include only 3,200 individuals. And in the most recent report of the Hanford study there are only 2,800 individuals exposed to 5 rems or more. I do believe, therefore, that the ORAU sample of DOE employees will in the end prove to have a dose distribution, and a total number of person-rems of exposure, that simply will not yield estimates in the low-dose region that will have enough stability to be very useful. I don't see how the study can solve what I call the low-dose problem.

Having said that, however, I would like to add that the study may help to rule out a level of risk that is, say, ten times the conventional risk estimates made by the United Nations Scientific Committee on the Effects of Atomic Radiation and by the Committee on the Biological Effects of Ionizing Radiation of the National Academy of Sciences. I would also add that I think we do need one or two, but not many, studies with that limited promise. My concern is that we not have too many; we should not think we can solve the low-dose problem by studying everyone with a known dose in that low range. The answer will not come that way, but rather through a better understanding of the mechanisms by which radiation produces untoward health effects, largely through experimental and theoretical work. What contribution will radiation epidemiology make to that better understanding? I suspect that it will be indirect and will operate in two ways:

(1) any theoretical formulation will have to be tested against the human data, and the more complex those data are the more rigorous the test will be; and

(2) increasingly human studies are pointing to unexplained sources of variation in risk that may suggest hypotheses to be tested in animal models or provide insights into more basic biologic processes.

With respect to gaps in our present knowledge other than the risk associated with low doses, I personally see little chance that the ORAU study will contribute effectively. And this is because I believe the number of radiogenic cancers that the investigators will have to work with will be so few, a handful or leukemias perhaps, a score or two of other fatal cancers. It is only when the number of excess cancers begins to pile up so that they can be subdivided to provide the basis for estimating differentials in risk that we begin to learn more than just that radiation produces cancer in yet another group. The A-bomb survivors, for example, provide an excess of about 90 deaths from leukemia and perhaps 160 deaths from other forms of cancer, through 1978. And the fact that the A-bomb survivor sample has about 40 excess incident cases of breast cancer underlies much of the recent advance in knowledge of the differential risks associated with age at exposure (probably hormonal state) and time since exposure. In a recent paper in Science (Sept. 12, 1980) Land has shown clearly why small studies with positive findings are so likely to be unreliable. Unless there are some unexpectedly large relative risks associated with important subsets of the ORAU material, or some major interaction with a chemical exposure, the DOE workers' experience will not produce new scientific information about ionizing radiation. Warnings not to expect much from low-dose studies appear in the Libassi report (Interagency Task Force on the Health Effects of Ionizing Radiation), the GAO report (Problems in Assessing the Cancer Risks of Low-Level Ionizing Radiation Exposure), the NAS FREIR report (Federal Research on the Biological and Health Effects of Ionizing Radiation), the NRC-EPA report on the Feasibility of Epidemiologic Investigations of the Health Effects of Low-Level Ionizing Radiation, and the Federal Strategy for Research into the Biological Effects of Ionizing Radiation. It is exposure at intermediate and high levels that is required to yield excess cases in sufficient numbers to generate new scientific knowledge, and the sample must be large enough.

I would, however, expect some information to come from the ORAU studies of exposure to agents other than ionizing radiation, and that there would be methodologic innovations of value. Preliminary reports have already been published on nickel and phosgene. The North Carolina group is very strong, and I cannot help but believe that it will react in creative fashion to the opportunity presented by the large accumulation of data. I think we can expect comparative analyses that will illuminate the potential of newer statistical methods in comparison with the more conventional ones and perhaps some innovations will prove useful in other studies. And the participation of the UNC group will undoubtedly influence the career choices of some of the students involved and thus strengthen the field of radiation epidemiology.

I regard the ORAU study as a defensive maneuver, undertaken in response to public and perhaps Congressional pressure, real or implied. With the level of public and hence Congressional concern that was building in the late 1970's, and the inability of authoritative scientific spokesmen to make adequately reassuring statements about the magnitude of the risks associated with exposures at the low-dose level, it was, I think, politically and socially necessary that one or two studies such as the ORAU study be undertaken as insurance against the chance that the conventional wisdom about these risks might be wrong in some major way. It is also my personal view that workers exposed to known toxic agents should be monitored for untoward health effects. Such monitoring may not require the elaborate study design and methodology of the ORAU study, but unless much of the rigor we associate with a good scientific study characterizes a monitoring effort the information will be unreliable.

2) Role of outside consultants in improving the epidemiology study.

(a) How could this mechanism be improved?

I have no specific knowledge of the way in which the outside consultants have interacted with the ORAU investigators.

3) How effective is the NIH Interagency Radiation Research Committee?

(a) How could it be improved?

Perhaps it is unnecessary to point out that the IRRC is not an NIH committee; although the Director of NIH was the first chairman, the Assistant Secretary for Health is presently the chairman, and in any event it is truly an interagency committee.

I have had very little experience with interagency committees and hence cannot compare the IRRC with other groups of this kind. The committee has been active, in one form or another, since January 1979, in partial response to PL 95-622 which directed the Secretary, HEW to (1) conduct a comprehensive review of current Federal research programs concerning the biological effects of ionizing radiation and (2) develop a comprehensive Federal program of research on the biological effects of low-level ionizing radiation. Federal agencies other than HEW were asked to participate in the work of the Committee on a voluntary basis, and the response was very positive. This Committee was established more formally on February 21, 1980, by President Carter in memoranda to the Secretary, HEW, and to the heads of other agencies. I think it has accomplished a great deal:

-- the Federal Strategy for Research into the Biological Effects of Ionizing Radiation has been developed on the basis of extensive input from the scientific community and a public meeting that was well attended

-- a critical review of federal research on the biological effects of ionizing radiation (the FREIR Report) has been made for the Committee by the National Academy of Sciences

-- the Committee responded to concerns about the burgeoning proposals for research on the residents of the area surrounding Three Mile Island following the TMI disaster in March, 1979.

-- a record was created and published concerning the Federal agency and Congressional activities of 1978-1980 leading to the formation of committees, task forces, and studies arising out of the public concern over the health risks associated with ionizing radiation

-- the pertinent Federal laws and regulations relating to the biological effects of ionizing radiation were brought together in a single document

-- the Committee reviewed the Report of the Panel of Experts on the Archive of PHS Documents Relating to Effects of Nuclear Weapons Testing on Health and evaluated its recommendations

-- the Committee reviewed a proposal by the Governors of Arizona, Nevada, and Utah to create a Tri-State Commission on the health effects of fallout from the atmospheric testing of nuclear weapons at the Nevada Test Site in the 1950's and early 1960's and subsequently reviewed grant requests from the Universities of Utah and Nevada and the Arizona Department of Health for the support of research on the health effects of that fallout; following disapproval of the grant requests arrangements were made for several of the agencies participating in the work of the Committee to fund those parts of the proposed research that were thought to have the highest priority and the greatest chance of success

- currently the Committee is devoting its efforts to planning the implementation of the Federal Strategy for Research into the Biological Effects of Ionizing Radiation and to a consideration of how far the individual agencies can go toward establishing common procedures for funding and managing radiation research, e.g., methods of scientific review of research proposals

As an observer of the Committee's activities I have been impressed by its leaders [illegible] quality of its main output. Meetings have been well attended and committees have responded effectively and promptly to their mandates. I regard the past three years as largely a period of organization and for the creation of tools for the effective pursuit of its mission. I have no suggestions as to how it could be improved.

4) Examination of the National Academy of Science's reviews of DOE's Study

(a) What recommendations have been implemented?

I have read the NAS report but have no knowledge of the steps that may have been taken to implement its recommendations.

I would be glad to answer any questions the Subcommittee may have concerning my testimony.

Mr. **Gore**. I appreciate the obvious time and effort you put into your response to our requests. I really appreciate it. We will withhold questions until the panel is completed.

Dr. Jablon, please proceed.

Dr. **Jablon**. Thank you, Mr. Chairman.

One of the penalties one pays for being the sixth witness in a panel like this is that almost everything that I had planned to say has already been said by one person or another and sometimes better, unfortunately, than I would say it myself.

Mr. **Gore**. We have five more witnesses, so if you feel inclined to summarize, go ahead.

Dr. **Jablon**. I have, of course, given you a written statement.

Mr. **Gore**. Without objection that will be included in the record.

Dr. **Jablon**. I will try to hit just the high points, if there are any.

My training is as a statistician, and for the past 30 years or more I have been working in the area of statistical epidemiology. I am director of the Medical Follow-Up Agency of the National Academy of Sciences National Research Council. Some additional information concerning my qualifications is appended to my written testimony.

I am, of course, speaking only for myself today, not for the National Academy of Sciences. Our panel has been asked to respond to your questions.

The first, reworded slightly, is at what radiation levels are studies such as that being done by ORAU scientifically meaningful? The cancer-inducing effects of ionizing radiation on man has been studied in a great variety of situations and a great deal is known about the carcinogenic effects of radiation at high doses. By high dose, I mean doses of say 50 rads or more. The results of all of these studies are by and large consistent.

From this very large body of data the United Nations Scientific Committee on the Effects of Nuclear Radiation in its 1977 report concluded that an average population of 1 million persons which were subjected to 1 rad of X-ray would during its remaining lifetime incur 100 to 150 extra fatal cancers resulting from the radiation.

The BEIR committee of the National Academy of Sciences reached a similar conclusion in its 1980 report. In a normal population of one million persons, about 180,000 will die of cancer. The extra deaths caused by one rad of radiation would constitute at most an increase of less than one-fifth of 1 percent in the number of cancer deaths over a lifetime.

I point this out to illustrate the difficulty of proving that an excess exists, let alone measuring it. Ordinary statistical variability will produce swings of 500, plus or minus, in the number of cancer deaths in a population of 1 million. Therefore, if we were to follow a population of one million for 50 years, at the end of that time we would very likely be uncertain that 250 extra cancer deaths had occurred even if they really did.

The UNSCEAR committee estimated the low dose and low dose effects may be only one of those seen at high doses. So perhaps only 100 extra deaths would occur and the probability of detecting them would become so small as to make the study of 1 million persons for 50 years a very bad investment, one almost predestined to failure.

The radiation levels of which epidemiological studies of the effects of ionizing radiation on populations are scientifically meaningful are those levels at which there is at least a reasonable chance that the adverse effects which are produced can be demonstrated to have occurred.

As a rough rule of thumb, the size of the population and the average dose must be such that the expected excess cancer mortality should be at least as large as the statistical uncertainty. Very roughly, if you are talking about one rad, you need about 3 million people; if you are talking about five, you need about 238,000; if you are talking about 50, you need something over 1,000.

It should be emphasized that the population sizes required are minimal: We have assumed that the radiation effects are probably larger than UNSCEAR or BEIR think they are; we assume that the populations are followed for their lifetimes, not for a mere 20 years; and even so, the statistical power obtained is not very great, there is only one chance in six of detecting an excess which is actually present.

The second topic is: The role of outside consultants in improving the epidemiology study and how can this mechanism be improved?

Outside consultants are always valuable for large, long-term studies. The investigators may become so immersed in solving the day-to-day and month-to-month problems that arise, they may be put so much attention into how to do things that they may omit to ask themselves why they are doing them and may not realize that events have occurred that point to the need for some change in strategy.

So, outside consultation is required. But in addition to consultants who are ordinarily simply reactive—responding to the questions and problems posed by the investigator—there is need for an oversight committee which meets on a regular basis, at least annually.

It should receive detailed progress reports; it should respond to questions asked by the investigator, but also volunteer advice concerning the conduct of the study when it feels that changes in procedures or program are advisable.

The committee should be made up of experts who are not employees of the funding agency or members of the institution conducting the study. Ideally, it will improve the research by its advice and counsel, but it will also serve as a monitoring group to insure that if things do not go well, those responsible will learn of problems in a timely way.

Your fourth question relates to the effect of this study by the NAS Committee on DOE Research on Health Effects of Ionizing Radiation. The committee's review of the ORAU study recommended, among others:

(1) Establishment of a continuing external review;

(2) Improved reliability and accuracy of follow-up information;

(3) Improved statistical design;

(4) Collection of data on factors such as smoking and other personal habits, and on morbidity; and

(5) Better coordination with other studies.

The committee prefaced its recommendations with the observation that the size of the population and the doses involved "represent populations too small to permit derivation of statistically significant information and conclusions, if the effects are about the same as expected on the basis of previous studies." Several people have said that today.

With respect to the first recommendation, it should be noted that the committee found that the program as a whole needed a uniform peer-review process by which all grant and contract proposals are evaluated at the time of submission and before renewal.

I am not aware that this recommendation has been implemented. This study does have a group of scientific consultants of excellent quality, but a consultative group is not a substitute for an independent, external peer review group.

Steps have been taken to fortify the mortality ascertainment process with other sources of information, such as drivers' licenses files, State death files and other files from which it is feasible to obtain information.

The third recommendation urged the improvement of statistical design. It appears to me that one consequence of the collaboration with the University of North Carolina group has been a great improvement in this area.

The collection of data on smoking, occupational exposures to chemicals, dusts and other hazards to health apart from radiation is underway. It is evident that the investigators both at ORAU and UNC are giving serious attention to methods of collecting and utilizing such data, and have made a good beginning at the process.

The last recommendation was for better coordination with other studies on health effects of ionizing radiation. I confess that the scope intended for this recommendation is not entirely clear to me. A death certificate retrieval office has been established at ORAU, intended to be an organization serving the needs of many studies as a way of introducing efficiency and of reducing costs.

I would now like to expand a little on my answer to your first question, "At what levels of radiation are such studies as that at ORAU scientifically meaningful?"

My opinion is that if one judges the value of a study solely in terms of the probability that new knowledge about radiation effects will be obtained, then the ORAU study would have to be judged as unlikely to succeed.

The academy committee reached the same conclusion. The average doses are too small for adverse effects to be detectable in a population of the order of 100,000 workers, even though effects may truly exist. Moreover, there is a danger in executing studies which are inherently incapable of detecting the small adverse effects which presumably are present, but hidden.

Investigators fractionate their material in every conceivable way, they examine each of several age groups, they divide the group up by length of employment, by whether or not internal dose monitoring was done, and each of these many subgroups is examined with respect to each of a dozen or more diseases.

Hundreds of comparisons, tests of significance are made. The mathematics of probability assures us that if we do, say, 200 different significance tests on a body of perfectly bland data, we shall find about 10 which are significant at the 5 percent level and 2 of them, probably, will be highly significant—at the 1 percent level—merely as the result of chance, random fluctuation.

The consequence of all this is that when we undertake a study which is too small we are almost guaranteed that not truth, but confusion, will emerge at the end.

Nevertheless, such studies must be done. The general public, the workers affected, do not read UNSCEAR or BEIR reports. There is skepticism regarding pronouncements by official bodies that certain exposure situations are safe. There is fear of the unknown and invisible, intensified by the general dread of cancer.

I do not see any way of dealing with such attitudes except by obtaining the data, counting the ill-effects and comparing them with those which occur in normal populations.

A good occupational medicine program in any industry will keep track of the health of the workers so as to discover as soon as possible any breakdown of safety precautions or unexpected effects.

It is in such terms that these studies can find their true justification, not in a Quixotic expectation that somehow contrary to the results of 30 years of epidemiologic investigation, we shall learn that the effects of radiation are ten or 20 times as large as we had thought.

[The prepared statement of Dr. Jablon follows:]

Testimony Before The

SUBCOMMITTEE ON INVESTIGATIONS AND OVERSIGHT
COMMITTEE ON SCIENCE AND TECHNOLOGY
U. S. HOUSE OF REPRESENTATIVES

May 19, 1982

Seymour Jablon

Testimony for Committee on Science and Technology
Subcommittee on Investigations and Oversight

May 19, 1982

Mr. Chairman, members of the Committee, I am very pleased to appear before you to discuss the Health and Mortality Study being conducted by the Oak Ridge Associated Universities for the Department of Energy.

My training is as a statistician and for the past thirty years or more I have been working in the area of statistical epidemiology - that is, the study of diseases in human populations with respect to problems of causation, treatment and outcome. I am the Director of the Medical Follow-up Agency of the National Academy of Sciences-National Research Council, and our Agency conducts studies of the kind I have just described. I also served for six years as Chief of the Department of Statistics and Epidemiology at the Atomic Bomb Casualty Commission, a field agency of the Academy which was responsible for the studies of the survivors of the bombings in Hiroshima and Nagasaki, Japan. I also am responsible for the Academy's participation in the Radiation Effects Research Foundation, a binational foundation established to continue the study of the Japanese A-bomb survivors. Some additional information concerning my qualifications is appended. I am, of course, speaking only for myself today, not for the National Academy of Sciences.

Our panel has been asked to respond to four questions. I am better qualified to respond to some of these than to others, but I know that other members of the panel will be able to cover the questions concerning which my own personal knowledge is inadequate. I have some additional comments which are related to two of your questions, but which go somewhat beyond their scope.

The first question, reworded slightly, is "At what radiation levels are studies such as that being done by ORAU scientifically meaningful?"

The answer to this depends upon whether it is sensible to approach a scientific question in a vacuum, ignoring all previous scientific work and all the knowledge that has been gained over a period of more than thirty years of studies on humans and an even longer period of studies on laboratory animals and other subhuman species. We obviously do not know all the answers at this time - perhaps we shall never answer all the questions that might be asked. But we do know a great deal. The cancer-inducing effects of ionizing radiation on man has been studied in a great variety of situations: in patients treated with large doses of X-ray as a treatment for the disease ankylosing spondylitis; in women treated by X-ray for certain conditions of the breast; among radium dial painters who ingested radium in the course of their work; among children who were irradiated for enlarged thymus glands; children who were irradiated in the treatment of ringworm of the scalp; among miners whose conditions of work exposed them to high concentrations of radon gas, and, not least, among atomic bomb survivors who were irradiated as a consequence of the atomic explosions. This list could be greatly expanded, but the message is clear. Very many studies have been made and, as a result, a great deal is known about the carcinogenic effects of radiation at high doses. By high doses, I mean doses of, say, 50 rads or more - the equivalent of, say, 2,000 chest X-rays. And it should be emphasized that the results of all of these studies are, by and large, consistent.

From this very large body of data the United Nations Scientific Committee on the Effects of Nuclear Radiation - the UNSCEAR Committee, in its 1977 report concluded that an average population of one million persons which was subjected to one rad of X-ray would, during its remaining lifetime, incur 100-250 extra fatal cancers resulting from the radiation. The Committee on the Biological Effects of Ionizing Radiation - the BEIR Committee - of the National Academy of Sciences reached a similar conclusion in its 1980 report. These estimates are based upon the assumption that, rad for rad, low doses are as harmful as large doses.

It is important to remember that nearly 20 percent of all deaths in the United States are attributable to cancer. In a normal population of one million persons, then, about 180,000 will die of cancer. The extra deaths caused by one rad of radiation would constitute at most an increase of less than one-fifth of one percent in the number of cancer deaths - over a lifetime. I point this out not to imply that 250 extra cancer deaths are unimportant - they are not - but to illustrate the difficulty of proving that an excess exists - let alone measuring it. Ordinary statistical variability will produce swings of 500, plus or minus, in the number of cancer deaths in a population of one million. Therefore, if we were to follow a population of one million for 50 years - an enormously expensive task - at the end of that time we would very likely be uncertain that 250 extra cancer deaths had occurred even if they really did.

I should emphasize further that both the UNSCEAR and BEIR Committees based their estimates on large radiation doses - not on doses of one rad. There is much experimental evidence that, at low doses of X-rays, effects are less than would be projected from data concerning high dose exposures. For this reason, the BEIR Committee declined to project its estimates to doses below ten rads, and the UNSCEAR Committee estimated that the low dose and low dose-rate effects might be only one-half of those seen at high doses. So, although even 250 extra cancer deaths, as we have already seen, would very likely be undetectably small against a baseline of about 180,000 total cancer deaths, perhaps only 100 would occur, and the probability of detecting them would become so small as to make the study of one million persons for 50 years a very bad investment - one almost predestined to failure.

The situation might be thought to be more promising if we are concerned not with all cancer but with leukemia. Leukemia is not a common disease. Less than one percent of deaths are attributed to leukemia in the general population, but the leukemia induction rate per rad is 25 to 50 per million according to UNSCEAR. In a population of one million exposed to one rad, 50 excess leukemia deaths might be induced, but they would be hidden in about 8,000 "naturally occurring" deaths from leukemia. It turns out that since the number of "baseline" cases is smaller, the sampling variability is relatively larger, and the population size requirements are identical for the detection of excess leukemia as for excess cancer in general.

Put We can now address explicitly the first question: The radiation levels at which epidemiological studies of the effects of ionizing radiation on populations are scientifically meaningful are those levels at which there is at least a reasonable chance that the adverse effects which are produced can be demonstrated to have occurred. As a rough rule of thumb, the size of the population and the average dose must be such that the expected excess cancer mortality should be at least as large as the statistical uncertainty - the statistical standard error - in the number of naturally occurring cancer cases. When the expected excess of cancer and the statistical uncertainty are equal, the probability of detecting that an excess is present will be only about one chance in six. There will be a parallel chance of one in six that the observed number of cancer deaths will actually be less than normal expectation. Very roughly, this works out as follows:

Average Radiation Dose (Rads)	Minimum Population Size Required
1	3,200,000
2	800,000
3	356,000
4	200,000
5	128,000
10	32,000
50	1,280

It should be emphasized that the population sizes required are minimal: We have assumed that the radiation effects are probably larger than UNSCEAR or BEIR think they are; we assume that the populations are followed for their lifetimes, not for a mere twenty years; and even so, the statistical power obtained is not very great - only one chance in six of detecting an excess which is actually present.

The second topic is: The role of outside consultants in improving the epidemiology study and how can this mechanism be improved?

Outside consultants are always valuable for large, long-term studies. Such studies tend to take on a life of their own; the investigators may become so immersed in solving the day to day and month to month problems that arise, they may put so much attention into how to do things that they may omit to ask themselves why they are doing them and may not realize that events have occurred that point to the need for some change in strategy.

Just how important outside consultation is for any particular study depends in part on the composition of the investigative team. A university group which includes members of strong departments of epidemiology and biostatistics, departments which are actively engaged in epidemiological research, will be less dependent upon outside consultants than will a group of investigators whose primary interest and expertise is in other areas, whether clinical medicine or radiobiology. My observation is that the strong epidemiological groups, which least require it, are the ones most aware of the value of consultation and which see that they get it. Unfortunately, experts in areas other than epidemiology and biostatistics, whether their area of expertise be pathology or occupational medicine or radiobiology, often fail to appreciate what it is they lack. After all, if you don't know that there is a problem you are not likely to seek advice on how to solve it.

So, outside consultation is required. But in addition to "consultants" who are ordinarily simply reactive - responding to questions and problems posed by the investigator - there is need for an oversight committee which meets on a regular basis - at least annually. It should receive detailed progress reports; it should respond to questions asked by the investigator but also volunteer advice concerning the conduct of the study when it feels that changes in procedures or program are advisable, even if that is not recognized by the investigator. The committee should be made up of experts who are not employees of the funding agency or members of the institution conducting the study. The members should be appointed by the funding agency; nominations should be sought from the investigator and from the agency program officer among others, but neither should be permitted to dominate the committee which, ideally, will improve the research by its advice and counsel, but which will also serve as a monitoring group to ensure that if things do not go well those responsible will learn of problems in a timely way.

Your third question concerns the NIH Interagency Radiation Research Committee. I have no personal knowledge of the workings of that committee and so cannot comment.

The fourth question relates to the review of this study by the NAS Committee on DoE Research on Health Effects of Ionizing Radiation. In 1980 that Committee reviewed the DoE program as a whole, and included the ORAU study specifically.

The Committee's review of the ORAU study recommended, among others:

1. Establishment of a continuing external review.
2. Improved reliability and accuracy of follow-up information.
3. Improved statistical design.

4. Collection of data on factors such as smoking and other personal habits, and on morbidity.
5. Better coordination with other studies on health effects of ionizing radiation.

The Committee prefaced its recommendations with the observation that the size of the population and the doses involved "represent populations too small to permit derivation of statistically significant information and conclusions, if the effects are about the same as expected on the basis of previous studies." I have documented, above, why this is true.

With respect to the first recommendation, it should be noted that the Committee found that the program as a whole needed a "uniform peer-review process by which all grant and contract proposals...are evaluated at the time of submission and before renewal."

I am not aware that this recommendation has been implemented. The study does have a group of scientific consultants of excellent quality but a consultative group is not a substitute for an independent, external peer review group.

As to the second point, steps have apparently been taken to fortify the mortality ascertainment process using Social Security records with other sources of information such as drivers' licenses files, state death files and other files from which it is feasible to obtain information.

The third recommendation urged the improvement of statistical design. It appears to me that one consequence of the collaboration with the University of North Carolina (UNC) group has been improvement in this area and further development of sophisticated statistical designs can be anticipated.

The collection of data on smoking, occupational exposures to chemicals, dusts, and other hazards to health apart from radiation is under way. It is easier to recommend that such data be acquired than it is to obtain it in objective, uniform ways. It is evident that the investigators, both at ORAU and UNC, are giving serious attention to methods of collecting and utilizing such data, and have made a good beginning at the process.

The last recommendation was for better coordination with other studies on health effects of ionizing radiation. I confess that the scope intended for this recommendation is not entirely clear to me. A Death Certificate Retrieval Office has been established at ORAU, intended to be an organization serving the needs of many studies as a way of introducing efficiency and of reducing costs. All investigator groups are, however, not necessarily satisfied to have an important part of their programs removed from their control, both as to quality assurance and scheduling. I have the impression that the existing difficulties could be greatly smoothed by better and more frequent inter-investigator communication. The Department of Energy has made a good beginning at improving communication by a conference of all investigators in mid-April of this year.

I would like now to expand somewhat on my answer to your first question - "At what levels of radiation are such studies as that at ORAU scientifically meaningful?" My opinion is, that if one judges the value of a study solely in terms of the probability that new knowledge about radiation effects will be obtained, then the

ORAU study would have to be judged as unlikely to succeed. The Academy committee reached the same conclusion. The average doses are too small for adverse effects to be detectable in a population of the order of 100,000 workers, even though effects may truly exist. The "background noise" of ill health which any population suffers is so much larger than the effect being sought that the effort seems fruitless. It is like trying to examine an atomic nucleus using a magnifying glass - the device has insufficient resolving power. Moreover, there is a danger in executing studies which are inherently incapable of detecting the small adverse effects which presumably are present, but hidden: In an attempt to be thorough, to overlook nothing, investigators fractionate their material in every conceivable way; they examine each of several age groups; they divide the group up by length of employment, by whether or not internal dose monitoring was done. And each of these many subgroups is examined with respect to each of a dozen or more diseases. In total, then, hundreds of comparisons, "tests of significance" are made. The mathematics of probability assures us that if we do, say, 200 different "significance tests" on a body of perfectly bland data, in which no true effects are present, we shall find about ten which are "significant" at the 5-percent level and two of them, probably, will be "highly significant" - at the 1-percent level - merely as the result of chance, random variations.

The consequence of all this is that when we undertake a study which is too small we are almost guaranteed that, not truth, but confusion, will emerge at the end. A better incitement to fruitless controversy could hardly be devised, as the melancholy history of the Hanford study illustrates.

Nevertheless, such studies must be done. The general public, the workers affected, do not read UNSCEAR or BEIR reports. There is skepticism regarding pronouncements by official bodies that certain exposure situations are "safe". There is fear of the unknown and invisible, intensified by the general dread of cancer. I do not see any way of dealing with such attitudes except by obtaining the data, counting the ill-effects and comparing them with those which occur in normal populations. A good occupational medicine program in any industry will keep track of the health of the workers, so as to discover as soon as possible any breakdown of safety precautions or unexpected effects. It is in such terms that these studies can find their true justification, not in a Quixotic expectation that somehow contrary to the results of thirty years of epidemiologic investigation, we shall learn that the effects of radiation are ten or twenty times as large as we had thought.

Mr. GORE. Thank you. You gave very interesting testimony.

Dr. Hutchison, in both 1980 and 1981 the reviewers cited a lack of overall scientific direction and recommended an overall study plan be developed.

What steps have been taken in your view to implement this recommendation?

Dr. HUTCHISON. This year—I think perhaps as a response to this suggestion or conceivably it was in the planning quite aside from our recommendation—the several Department of Energy groups at Oak Ridge and at the other facilities held a large meeting, which unfortunately I was not able to attend, that did in fact pull together work of I believe all of these Department of Energy studies.

The suggestion that our advisory group made was subject to a variety of interpretations. One interpretation was that it meant the technologies should be better coordinated; for example, that the death certificate search should be done in a coordinated fashion for all of the studies. That had already, in fact, been done and that wasn't what we had in mind in the recommendation.

The recommendation, at least as I myself saw it, was that an attempt should be made to pull together the findings from all of these studies, either at present insofar as findings are available, or in some early future time when more findings would be available to attempt to give an overall statement from the combined material of all of these studies.

I principally was thinking of the Oak Ridge studies, but I was very pleased to think that that was interpreted to refer to indeed all of the Department of Energy studies.

Mr. **Gore**. Now, your committee also recommended scientific leadership to lead this study. In view of your comments, do you still believe that, and why do you say that?

Dr. **Hutchison**. I am a little puzzled by your question, Mr. Chairman. I didn't know that anyone had doubted that the group needed a scientific leader.

Mr. **Gore**. Well, the emphasis is on the word scientific. In 1981, the first recommendation is to continue efforts to obtain a full-time leader or scientific director?

Dr. **Hutchison**. Yes; I understand the recommendation, which has been repeatedly made. My puzzlement was that I don't believe the group at Oak Ridge has ever questioned that they need that. Indeed, Dr. Lushbaugh has led an active effort to find such a leader and the administration over Dr. Lushbaugh has similarly, for a number of years, been attempting to place a person in the position of leadership of this operation.

It has been a very difficult search. To date, as I understand it, there hasn't been a suitable person found. But to my knowledge no one has doubted that there was a need to have such an appointment.

Mr. **Gore**. How long do you think the study should continue?

Dr. **Hutchison**. We had some earlier discussion this afternoon about that question. In line with my earlier comments, that relates very heavily to the mandate that one sees for this group of studies. If they could be viewed as purely scientific studies, as might be elected to be done by a university research department, they certainly would be stated within a finite time period to collect a previously stated number of individuals and number of person years of followup of these individuals relative to specific research questions.

If it is not viewed in that fashion, but if the mandate of the Department of Energy is more in the nature of surveillance, as I described my interpretation of it in my comments, then it is an ever-continuing operation.

The difficulty that I have with it is that I don't find a clear distinction, as I envision the operation, as to which of these activities it is to be viewed as. If that could be clearly determined, then any scientific studies would have a clear, finite ending. A surveillance operation would continue indefinitely, just as surveillance in occupational health continues indefinitely in all major industries in this country and in the industrialized world.

Mr. **Gore**. Dr. Beebe, you also seem somewhat pessimistic about epidemiological studies of people exposed to low-level ionizing radiation.

Do you think in light of that view, which you hold, that this study ought to have a logical conclusion, that we ought to change the structure of it or that it should continue as an open-ended effort which Dr. Hutchison, for one, characterizes as a surveillance effort?

Dr. **Beebe**. I think the very positive aspects of this study have to do with monitoring or surveillance. I see no hope for that except that it be a continuing operation.

I am one with Dr. Hutchison in his view that you can't put the 5-year term on it, but in saying that, I don't want to stress too much continuation of the study as presented here because a survey designed for a surveillance only might differ from the study as we know it today.

But certainly an effort along these lines is very much needed. I am in no position to judge the budget. I am not about to say you could do surveillance for half the price, but it seems to me that if it is planned as surveillance, it may not look to be exactly what it is today.

Mr. GORE. You have outlined some approaches to improving our knowledge about low-level ionizing of radiation effects. You outline nine factors to be taken into account in your prepared remarks. Are there any specific studies underway that take those nine factors into account?

Dr. BEEBE. I don't want to be misunderstood about the meaning of that list. This has to do with radiation epidemiology generally. It is not aimed specifically at low dose.

What I am saying in general about low dose is that the answer with respect to low dose risks is going to come from other research. The one item on the list that is an acknowledged purpose of the ORAU study, is the low-dose problem, this is a real problem, but I can't expect the ORAU study to make an important contribution to it, either with respect to the mathematical form of the dose—response function or directly.

There is another aspect of my list which is perhaps of considerable significance for the ORAU study; that is, the detection of an interaction between chemical exposure and ionizing radiation.

If there are such interactions, the ORAU study might make an important contribution. You would have to ask someone like Dr. Upton how realistic that is.

Mr. GORE. We will ask him on the next panel.

Dr. Jablon, given the lack of empirical knowledge about the low-level ionizing radiation effects, or the imperfect nature of it, what do you suggest be done in the Federal Establishment to improve our knowledge?

Dr. JABLON. Well, I agree with what I think Dr. Beebe was saying. My opinion is that we are going to know about low-dose radiation effects when we understand better just what it is that is happening in the cell, when ionization processes take place.

Is the fundamental intracellular defect an exchange aberration in a chromosome? What is it? When we know exactly what is happening, I think we will be able to figure out well enough from our knowledge of what gamma rays do, what electrons do, what neutrons do, within nuclei, to be able to deduce how the response relationship should go, and we will then be able to test such relationships against observational material at higher doses.

So, by playing back and forth between the theory and the observation, we may become fairly secure in what we think we know about radiation of low doses. Well, I will stop there.

Mr. GORE. Basically, all of you are saying that this pool of data about Federal workers exposed to radiation, is not in your view the gold mine of the data that a lot of people think it is, and that the ability to elicit or extrude significant findings from that pool of data is quite limited? Is that what you are saying?

Dr. **Jablon**. I personally believe that to be true. Yet, I think we have to do it anyhow because we have to distinguish between our hopes for new scientific information, which may be appreciated by and wanted by a relatively small fraction of the population, and the general public, both those who are directly concerned and others who are mistrustful and who I think, if they are to be convinced, will only be convinced by putting the data on the table.

Mr. **Gore**. Dr. Beebe, same question.

Dr. **Beebe**. I agree with your statement also if you qualify it with respect to ionizing radiation because there may be other truly scientific goals there. I am not an expert in occupational medicine. I don't know how important some of these chemical things are, but they look good to me as I read the material.

Mr. **Gore**. Dr. Hutchison?

Dr. **Hutchison**. Yes, I agree.

Mr. **Gore**. All right. I want to thank you all for your patience and for your contribution here. Thank you very, very much. Obviously you put a lot of time into it, and it will help us come to some conclusions about this.

Thank you so much.

Let me call the next panel to come forward: Dr. Arthur Upton, chairman of the Department of Environmental Medicine at New York University Medical School; Dr. William Halperin, Chief of the Industry-Wide Studies Branch of the National Institute for Occupational Health; Dr. William F. Brandom, Department of Biological Sciences at the University of Denver; and Dr. Sidney Marks, Battelle Pacific Northwest Laboratory with the environmental health and safety research program.

Gentlemen, if you would stand and raise your right hand, please.

[Witnesses sworn.]

Mr. **Gore**. Thank you very much.

Before recognizing the witnesses, I would like to call on my colleague, a member of the full committee and chairman of the Energy Research and Production Subcommittee, the Honorable Marilyn Bouquard.

Mrs. **Bouquard**. Thank you very much, Mr. Chairman. It is a pleasure to be with you today.

As you know, the Energy Research and Production Subcommittee has had continuing interest in the health effects of low-level ionizing radiation in line with our jurisdiction over nuclear energy R&D.

We did hold 3 days of hearings on this topic in June of 1979. Our findings at that time were essentially consistent with the major thrust of the testimony to be presented today.

The health effects of ionizing radiation are still better understood than are the effects of many toxic substances carefully used and produced by industrial processes. Quantification of health effects at low exposure levels is still very difficult and controversial, and the public reception of radiation risks still engenders a level of concern that is unsupported by the best research results we have to offer.

One of the expert witnesses that testified at our previous hearings is Dr. Sidney Marks. He is participating today on the third panel, addressing future research efforts, and provides a measure of continuity for the community.

It is nice to see you again, Dr. Marks, and I am sure you will make a very valuable contribution in this hearing, as you did in ours several years ago.

Thank you very much.

Mr. **Gore**. Thank you very much.

Why don't we begin with you then, Dr. Marks.

Welcome to the subcommittee. We are delighted to have you here. Without objection, your entire text will be included in full in the record.

I apologize for the length of these proceedings, as I do to all of the witnesses, but I appreciate your patience and forebearance and invite you to proceed.

STATEMENT OF DR. SIDNEY MARKS, BATTELLE PACIFIC NORTHWEST LABORATORY, ENVIRONMENT, HEALTH AND SAFETY RESEARCH PROGRAM; DR. ARTHUR UPTON, CHAIRMAN, DEPARTMENT OF ENVIRONMENTAL MEDICINE, NEW YORK UNIVERSITY MEDICAL SCHOOL; DR. WILLIAM HALPERIN, CHIEF, INDUSTRY-WIDE STUDIES BRANCH, NATIONAL INSTITUTE FOR OCCUPATIONAL SAFETY AND HEALTH, AND DR. WILLIAM F. BRANDOM, DEPARTMENT OF BIOLOGICAL SCIENCES, UNIVERSITY OF DENVER

Dr. **Marks**. Thank you, Mr. Chairman. Thank you, Mrs. Bouquard.

I will omit a few paragraphs from my written testimony for the sake of time, including the first paragraph.

In addressing the future of the DOE radiation epidemiology program, questions that occur to me are whether the studies of workers are worthwhile, what purposes they serve and what can be done to strengthen them? These are in addition to issues raised by the subcommittee staffs.

I firmly believe that the DOE-sponsored worker studies have been exceedingly important and have contributed in a manner totally out of proportion to the expenditures on such studies.

These studies were criticized from the very beginning for having too little statistical power; that is to say, the levels of radiation exposure to the workers are so low that the few cases of cancer that might be caused by radiation in these populations may not be demonstrable statistically. Therefore, we hear the words, because of this, don't do these studies.

I acknowledge that the statistical power of these studies tend to be low. However, I have found in my personal experience, which is shared by many others, that sometimes irresponsible investigators study small segments of a worker population or use other improper statistical techniques or happen upon a few cases of a disease, a so-called cluster; then they arrive at conclusions of enormous cancer risk and then generalize to the whole population of workers.

These findings of potential health damage greatly in excess of what is considered an acceptable risk are terrifying to workers and their families, and then those fears spread to the general public.

In an ideal world peopled exclusively by sophisticated radiobiologists, if there were an ideal world we could dismiss these findings as incompatible with our best thinking and, therefore, deserving of no further consideration.

In our real world, the workers and their families can only be reassured by the results of well-conducted studies on the workers themselves. Our personal experience at the Hanford plant is that the local population, including the workers, will accept the results of responsible studies.

In the absence of such studies, they would be seriously troubled by aberrant estimates of hazards to their health, estimates that may be disregarded as a fluke or dismissed out of hand by the responsible scientific community.

I urge the continued sponsorship by DOE of such studies, and even the expansion of this program where need for additional studies is identified. They will never be funded by NIH or NSF. On the other hand, they are an important part of the DOE mission.

I plead for the incluson of societal need as a criterion in judging the merit of such studies and their qualification for funding.

With respect to the accomplishments of these studies, the data on our Hanford population have probably been studied most extensively. I believe that despite its low statistical power, this study does now and will continue to provide data of scientific value.

For the most part, the study has demonstrated compatibility with the low-risk estimates projected for this low-dose population from studies at higher doses, such as those of the A-bomb survivors.

On the other hand, an apparent relationship of radiation exposure to multiple myeloma, an uncommon cancer type, was demonstrated in this population several years ago. It was initially regarded as aberrant finding but was subsequently seen in workers at the Windscale Plant in the United Kingdom and also in the Japanese survivor population.

A more tenuous relationship of radiation to cancer of the pancreas was observed in our population earlier but has disappeared in our latest analysis, which includes more recent deaths.

I believe that these results, including the verification of the order of risk at low doses, based on best available risk estimates, qualify as scientifically important.

Exposure to radiation is vastly easier to measure and more reliable than exposure to other potentially hazardous agents, such as chemicals. Working with our radiation exposure data set and an excellent body of plant personnel data, Dr. Ethel Gilbert, our statistician, received a national award from the American Statistical Association in 1979 for her paper on the methodology of analyzing health effects in occupational populations.

I view this as a scientific contribution which will be repeated many times over in other studies in this DOE radiation epidemiology program as data collection is completed in the various studies.

To turn to some of the issues raised by the subcommittee, the study of chromosomal abnormalities should be encouraged but not necessarily as a major element in epidemiologic studies, at least at this point.

We must first see a quantitative relationship established between chromosome aberrations and cancer or other health effects before redirecting our efforts from the study of disease to the study of chromosomes. The defining of such relationships might even be better accomplished in experimental animal than in human studies.

The occurrence of chromosomal abnormalities at low radiation levels of itself does not imply any special risk to people if we cannot relate the chromosomal changes to cancer risk.

If we were to reach the stage at which chromosome aberrations are a quantitatively adequate surrogate for cancer, we would then have grounds for making chromosome studies a key element of our epidemiologic program.

On the question of further university involvement in the epidemiologic program, I would point out that there are advantages and disadvantages to both universities and DOE-sponsored laboratories.

It is certainly desirable to take advantage of the talents of many university faculty members like Dr. Shy, Dr. Hutchison, and Dr. Upton, by placing studies in their departments. Furthermore, the involvement of graduate studies in such studies is a means of training future epidemiologists and interesting them in this field.

However, there is a certain risk in that some faculty members who spend much of their time teaching may provide insufficient guidance to their graduate students to achieve output of the best quality.

Furthermore, in studies conducted over a period of many years, like those of nuclear workers, a data set may lose its instructional value at some point; in other words, it may be milked dry. In that case the university may give up on the study or relegate it to less qualified personnel.

The laboratories have studied several relevant populations for some time but have not embarked on major epidemiologic programs until recently so that they do not have long records of accomplishment.

Their advantages are that the staffs are dedicated in the sense of being able to devote all or a major share of their time to the epidemiology projects. They are also in a better position to undertake interdisciplinary efforts because the laboratory discipline requires a willingness to participate actively in joint activities. This becomes especially important when a study may require the joint effort of epidemiologists, biostatisticians, health physicists, and data managers.

The university quite properly encourages individual excellence. In any event, some studies are best done in universities while others are accomplished more effectively in laboratories.

What should the future of the program be? Despite the appeal of proposing bold new thrusts, I believe that the future course of this program should lie in strengthening the existing program, which is already headed in the right direction.

The basic studies that have made extrapolation from high to low radiation levels meaningful should be encouraged and funded as in the past. These studies have contributed vital information on the interaction of radiation with matter, dose-rate effects, differences in the response of biological systems to low- and high-level linear-energy-transfer radiation and many other aspects of these problems.

I believe that the extremely important work on the A bomb survivors should be continued until all useful information will have been extracted from this immense, expanding, and, we hope, unique data set.

Finally, the epidemiologic surveillance to accompany the medical surveillance of nuclear workers at selected facilities should be continued so that an increasing body of direct observations will be available at low radiation levels and so that we can respond to the anxieties of workers and their families.

I do have a couple of suggestions for projects that although not new conceptually are not being implemented.

A national workers radiation registry that would compile annual radiation doses from all sources, including NRC licensees, would be highly desirable. Such a registry would be complex and expensive, but would mitigate the problem in analyzing data at any plant of attributing to the individual the radiation dose he receives at that point and perhaps that incurred in the course of his earlier work, but we never get the dose he received after leaving the plant. A national registry would correct this deficiency.

A lifetime limit on exposure has been proposed. If it were adopted, such a registry would be essential to make the limit meaningful. I learned today there is some effort being made in the effort to this national registry that Dr. Goldstein could address.

A second problem that needs to be addressed more adequately is the probem of radon daughter exposure. This problem is of truly massive proportions. It affects the general public, as well as uranium miners.

In a narrow sense, it does not fall into the scope of DOE because the DOE community does not include uranium miners, but insofar as DOE is the principal organ of Government sponsoring radiation health research, it is an appropriate area for DOE to investigate.

The data base for estimating radon daughter effects was developed largely for exposures that occurred in an early period when conditions were poorly controlled in mines and exposures were very large.

Studies of lower exposures have been conducted in other countries, but in some cases at least we have little access to those data. If this were a lesser problem, studies that have been conducted already would be sufficient.

However, the implications of radon daughter exposure are enormous. The potential for health damage is greater among miners than in any other segment of the nuclear industry and, conversely, the economic implications of unwarranted limitation of exposure are severe.

Beyond that, limiting air exchange in houses as a conservation measure has begun and will continue, especially as energy prices rise again.

We hear dire predictions of increased deaths due to lung cancer from the buildup of radon daughters in houses or other buildings.

At this moment the epidemiologic study of such residential exposure appears to be extremely difficult.

So, we must fall back on the study of uranium miners, especially those who experienced low or intermediate levels of exposure, for information to use in evaluating the radon daughter problem for the miners and for the exposure in their homes of ordinary citizens not connected with the nuclear industry.

I do not have specific recommendations in this regard, but I do feel that DOE should look deeply into this matter and consider funding any studies that need to be done to clarify this difficult issue.

Mr. Chairman, thank you for the opportunity to discuss these matters at this hearing.

[The prepared statement of Dr. Marks follows:]

TESTIMONY BY
SIDNEY MARKS
PACIFIC NORTHWEST LABORATORY
OPERATED BY BATTELLE MEMORIAL INSTITUTE
RICHLAND, WASHINGTON 99352

FOR THE
HEARING ON EPIDEMIOLOGIC INVESTIGATIONS OF THE
HEALTH EFFECTS OF LOW-LEVEL IONIZING RADIATION
BY THE SUBCOMMITTEE ON INVESTIGATIONS AND OVERSIGHT
AND THE SUBCOMMITTEE ON ENERGY RESEARCH AND PRODUCTION
OF THE COMMITTEE ON SCIENCE AND TECHNOLOGY
OF THE U.S. HOUSE OF REPRESENTATIVES

May 19, 1982

TESTIMONY BY
SIDNEY MARKS

PACIFIC NORTHWEST LABORATORY
OPERATED BY BATTELLE MEMORIAL INSTITUTE
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In my testimony today, I wish to discuss the DOE radiation epidemiology program in terms of the mission of the department and the future course of the radiation epidemiology program that will best serve that mission. Historically, DOE is a direct descendant of the AEC, which set out initially to investigate the impacts of radiation on matter, biological systems and the environment. Very early, the AEC provided funding to and actively promoted the development of the Atomic Bomb Casualty Commission, which, with its successor organization, the Radiation Effects Research Foundation has been the most important source of information on late effects of radiation on human beings. It also sponsored the equally important and successful study of Marshallese who were exposed to fallout from a nuclear test in 1954 and the radium dial painters. Only later, in 1964 and subsequent years, did the AEC develop a broad radiation epidemiology program. The start of the AEC Health and Mortality Study in 1964, perhaps indirectly, initiated the role of AEC in studying the possible impacts of an energy source, in this case nuclear energy. Since then, a strong program directed to the study of workers exposed to radiation in the industry has developed. It now includes studies of workers exposed to external radiation or plutonium in DOE facilities, naval shipyard workers and other groups who will probably have been identified for you already.

In addressing the future of the DOE radiation epidemiology program, questions that occur to me are whether the studies of workers are worthwhile, what purposes they serve and what can be done to strengthen them. These are in addition to issues raised by the subcommittee staffs.

I firmly believe that the worker studies have been exceedingly important and have contributed in a manner totally out of proportion to the expenditures on such studies. These studies were criticized from the very beginning for having too little statistical power. That is to say, the levels of radiation exposure to the workers are so low that the few cases of cancer that might be caused by radiation in these populations may not be demonstrable statistically. Therefore, we hear the words, don't do these studies. I acknowledge that the statistical power of these studies tends to be low. However, I have found in my personal experience, which is shared by many others, that sometimes, irresponsible investigators study small segments of a worker population or use improper statistical techniques or happen upon a few cases of a disease, a so-called cluster, arrive at conclusions of enormous cancer risk and then generalize to the whole population of workers. These findings of potential health damage greatly in excess of what is considered an acceptable risk are terrifying to workers and their families, and those fears spread to the general public. In an ideal world peopled exclusively by sophisticated radiobiologists, we could dismiss these findings as incompatible with our best thinking and, therefore, deserving of no further consideration. In our real world, the workers and their families will only be reassured by the results of well-conducted studies on the workers themselves. Our personal experience at the Hanford plant is that the local population, including the workers, will accept the results of responsible studies. In the absence of such studies, they would be seriously troubled by aberrant estimates of hazards to their health, estimates that may be disregarded as a fluke or dismissed out of hand by the responsible scientific community.

I urge the continued sponsorship by DOE of such studies and even the expansion of this program where need for additional studies is identified. They will never be funded by NIH or NSF; on the other hand, they are an important part of the DOE mission. I plead for the inclusion of societal need as a criterion in judging the merit of such studies and their qualification for funding.

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Exposure to radiation is vastly easier to measure than exposure to other potentially hazardous agents such as chemicals. Working with our radiation exposure data set and an excellent body of plant personnel data, Dr. Ethel Gilbert, our statistician, received a national award from the American Statistical Association in 1979 for her paper on the methodology of analyzing health effects in occupational populations. I view her work as an important scientific contribution, which will be repeated over time in other studies in this DOE radiation epidemiology program as data collection is completed in the various studies.

With regard to medical surveillance and studies, I would not wish to see any sweeping changes in the form of new directions or new thrusts. Medical surveillance in DOE-operated facilities is probably the equal of any in the world. Epidemiologic studies of the workers should be conducted with best available epidemiologic techniques, using special procedures, such as kidney studies, only when indicated. Such studies may be important to the scientific investigation of persons who have been exposed to high levels of uranium, because of possible toxic effects of uranium on the kidneys. For that reason, kidney studies may be appropriate for some oldtimers in plants where uranium was processed during wartime, but these studies would not be purposeful in more recent employees or in plants where there has been little handling of uranium. The use of special techniques should be considered on a case-by-case basis, and future developments should be directed to incorporating the data accumulated in medical surveillance programs into the data bases that are used in epidemiologic studies. To some extent that process is going on now, but it could be reinforced.

The study of chromosomal abnormalities should be encouraged but not necessarily as a major element in epidemiologic studies, at least at this point. We must first see a quantitative relationship established between chromosome aberrations and cancer or other health effects before redirecting our effort from the study of disease to the study of chromosomes. The defining of such relationships might even be better accomplished in experimental animal than in human studies. The occurrence of chromosomal abnormalities at low radiation levels of itself does not imply any special risk to people if we cannot relate the chromosomal changes to cancer risk. If we were to reach the stage at which chromosome aberrations are a quantitatively adequate surrogate for cancer, we would then have grounds for making chromosome studies a key element of our epidemiologic program.

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I believe that the extremely important work on the A-bomb survivors should be continued until all useful information will have been extracted from this immense, expanding and, we hope, unique data set. Finally, the epidemiologic surveillance to accompany the medical surveillance of nuclear workers at selected facilities should be continued so that an increasing body of direct observations will be available at low radiation levels and so that we can respond to the anxieties of workers and their families.

I do have a couple of suggestions for projects that, although not new conceptually, are not being implemented. A national workers radiation registry that would compile annual radiation doses from all sources, including NRC licensees, would be highly desirable. Such a registry would be complex and expensive but would mitigate the problem in analyzing data at any plant of attributing to the individual the radiation dose received at that plant and, perhaps, that incurred in the course of his earlier work but never the dose he received after leaving the plant. A national registry would correct this deficiency. A lifetime limit on exposure has been proposed. If it were adopted, such a registry would be essential to make the limit meaningful.

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Mr. Chairman, thank you for the opportunity to discuss these matters at this hearing.

Mr. GORE. Thank you very much. I appreciate it. I will withhold questions until we complete the panel.

I would like to call now on Dr. Arthur Upton, chairman of the department of environmental medicine at NYU.

Dr. Upton, let me depart from the schedule for just a moment and ask you a question before you deliver your testimony on this subject. Let me explain that this subcommittee is holding a hearing tomorrow on a different subject and because of your expertise in this area, I want to ask you one brief question for the record in preparation for tomorrow.

We are holding a hearing to review the scientific basis of the Environmental Protection Agency formaldehyde risk assessment procedure. You are on record as stating that formaldehyde is a potential human carcinogen based on animal studies. Is that correct?

Dr. UPTON. Yes, Mr. Chairman. I should stress at the outset that I have not personally worked with formaldehyde. I do not consider myself to be an authority on formaldehyde toxicology.

Mr. GORE. Fine. Can you comment briefly on what led to your opinion in this regard?

Dr. UPTON. Yes, Mr. Chairman. Studies were undertaken in my department some years ago under the direction of Dr. Norton Nelson, my predecessor as director of the institute, and Dr. Roy Elbert, a professor in the department who continues the studies in question.

It was on the basis of these studies, which had not yet been published in full, that I had written to regulatory agencies concerning the as yet unpublished data to make them aware of what I consider to be unequivocal evidence of carcinogenicity of formaldehyde in our animals.

Mr. GORE. Unequivocal.

And if you are familiar with Dr. Todd Hunter's February 10, 1982, explanation of EPA's decision on formaldehyde, do you find Dr. Todd Hunter's evaluation of the scientific evidence convincing and do you believe they are widely accepted in the scientific community?

Dr. UPTON. Again, Mr. Chairman, I have not gone through Mr. Todd Hunter's statement and evaluation in fine detail.

I have read it and I must confess that I do not find it convincing. I take issue with its contention that the carcinogenicity of formaldehyde is not sufficiently demonstrated in animal studies.

I think it has been convincingly demonstrated in animal studies and I don't follow the argument. Such extrapolations that he has made indicate no potential threat to human populations.

In fact, I think there are contradictions in the arguments he gives. Some of his calculations indicate risks on the order of one in a thousand for cancer in certain occupational exposure for the population .

How he considers these to be somehow no adequate evidence of human risk, I don't understand.

Mr. GORE. What levels of risk have been traditionally regarded as cause for concern by Federal agencies?

Dr. UPTON. I am not experienced in regulatory matters, so, again, I would not feel this is a subject I can comment on authoritatively.

In general, one is concerned with risks that cause substantial numbers of serious injuries or death.

If we are talking about thousands of deaths in a population, each year this is a significant and serious matter.

Mr. GORE. In a population the size of our country's population?

Dr. UPTON. Exactly. For this reason a risk of the individual of the order of 1 in 10,000 or 1 in 1 million becomes a significant problem if it affects 200 million people in the population.

Mr. GORE. So you would say one in a million would be significant?

Dr. UPTON. In general, I would think that when we are speaking about risks to the general population we are concerned that risks in the order of 1 in 100,000 or 1 in 1 million.

Mr. GORE. One in 100,000 or 1 in 1 million; that order of magnitude?

Dr. UPTON. Yes.

Mr. GORE. You would say 1 times 10 to the minus 1?

Dr. UPTON. One times 10 to the minus 1 is a risk of 1 in 10. That is a very large risk.

Mr. GORE. You would say that is an extremely large risk?

Dr. UPTON. Indeed.

Mr. GORE. One in 100,000 is 1 times 10 to the minus 4?

Dr. UPTON. One times 10 to the minus 5, 5 zeros.

Mr. GORE. Okay, I think I am catching on here. So, 1 times 10 to the minus 5 would be a significant risk?

Dr. UPTON. For regulatory purposes; yes.

I think a regulatory agency would be concerned about a risk on that order; yes.

Mr. GORE. How comparable is that sort of risk to the risk that you believe is present where low-level ionizing radiation is involved?

Dr. UPTON. If we take the estimates of the Advisory Committee on Biological Effects of Ionizing Radiation published by the National Academy, my recollection is the estimates would suggest that on the order of 1 percent of cancers are attributable to natural background.

There are 400,000 deaths per year in cancer in the United States today; roughly 400,000. One percent of this would be 4,000. So these are 1 times 10 to the minus 2, if you will, of the naturally occurring incidents.

Mr. GORE. I would like to recognize counsel for the minority.

Mr. CLEMENT. No questions.

Mr. GORE. Proceed with your statement, then. I apologize for that digression but we will be getting into that in great detail tomorrow, including what you indicate are apparent contradictions in Dr. Todd Hunter's statements. Others will disagree, but please proceed.

Dr. UPTON. I am pleased and honored to testify since I have submitted a written statement for the record. In view of the hour I would like to simply touch on highlights.

At the outset, I would want to emphasize that I have devoted much of my career to the study of radiation injury with particular reference to the effects of low levels of radiation.

As has been brought out repeatedly before you this afternoon, despite the wealth of information we have about radiation effects and the fact that the effects of ionizing radiation are better known than those of any other physical or chemical agent, we still have uncertainty about the risks of low-level radiation, concern about them and need to refine our ability to assess these risks.

So, further study is clearly called for.

The risks about which we are particularly concerned are the mutagenic effect, carcinogenic effects and the effects on the growth and development of the employee.

I can scarcely add to the conclusions of other expert study groups who have looked at the problem. I refer to studies that have been published within the last year or two by the Controller General, by the Department of Health and Human Services, by the National Academy of Sciences.

All of these studies agree on the conclusion that to address the problem in a broad spectrum of approaches will be necessary.

You cannot rely on brute force epidemiological approaches alone.

On the other hand, our estimate can only be validated by observations in humans. So there is a role for epidemiological studies but because the epidemiological studies are relatively insensitive it is not going to be scientifically productive to attempt to examine all the populations exposed to low levels. Rather, one should select carefully those populations in whom the dose is large enough and well enough defined and the health-effects data are likely to be well enough documented to enable a scientifically useful dose-effect assessment.

Here I think the atomic bomb survivors represent a population that must be studied further if we are going to find out about the effects on cancer incidence in individuals exposed early in life.

They are just now reaching the cancer range and we have got to follow them another 20 or 30 years.

The new technology in the evaluation of the mutagenics may warrant the research of genetic effects in the next several years depending on the development in that area even though all efforts to date have been negative.

Some of the occupations-exposed populations are clearly well worth studying and I would support the statements that have been made by others who have testified this afternoon with reference to the Oak Ridge study.

We obviously can't afford to neglect these opportunities. We have a scientific interest in them and we have a moral commitment to the exposed individual.

Insofar as laboratory studies are concerned, these need to be conducted so that we can, as Mr. Jablon pointed out, begin to understand more adequately what is happening in irradiated cells, what are the mechanisms that give rise to what we are interested in.

We need to develop bases, principles with which we can make more confident extrapolations to get at the shape of the mathematical curve, as Dr. Beebe pointed out.

So not simply the total dose but the way the dose is distributed in space and in time—these are factors that we need to understand better in animal models.

The behavior of radio nuclides, Dr. Hanz mentioned this. Animal studies can also be very helpful on this. The whole spectrum of modifying variables.

The influence of differences in genetic background, species, strains, sets, age at irradiation, differences among different organs and cells within the organ, influence of physiological variables, the interactive effects of chemicals, drugs, hormones, other physical agents such as heat, ultraviolet light, the role of repair processes, our ability to reverse such effects is becoming evident now.

Mr. GORE. Dr. Upton, I am going to have to ask you to suspend. The committee has another close vote on the floor on another Walker amendment. I am sorry. There is nothing I can do about it. It will be another 5 to 7 minutes.

[Brief recess.]

Mr. GORE. The subcommittee will come back to order.

Gentlemen, I fear my apologies are wearing thin. The subcommittees all over the Hill have been disrupted this afternoon. It is one of those unusual days when you have a series of very close votes. This last one was a tie vote, 193 to 193 and that is the way it has been.

So I apologize to you and for those who have been so patient I just tell you that we appreciate that patience and if we could summarize from here on out I think it would probably be best.

Dr. Upton, you were on the last page of your statement.

Dr. UPTON. Yes, Mr. Chairman, I will try to summarize and close very quickly.

I was emphasizing that most authorities agree that there need to be approaches at virtually every level of biological organization, and that these can be expected to be highly productive by virtue of the accuracy and sensitivity with which we can measure radiation doses and the wealth of existing knowledge.

It is possible to foresee that with further study we can really begin to get at the heart of these problems and, hence, not only our understanding of radiation injury but, again, new understanding of many basic biological processes and the effects of agents other than radiation as well.

As concerns the question of the role or the place of medical surveillance, this is not my area of expertise. It is my impression from a distant vantage point on the subject that we are still groping for the tools with which we can predict the outcome of the radiation exposures or exposures to chemicals.

This is a research salient. There are yet no established techniques that one can apply in epidemiological studies to large populations that can be valuable.

Obviously, one should watch this field and take advantage of opportunities as they present themselves.

The studies must clearly exploit insofar as possible the special strengths of university-based research, the great diversity of talents. Many disciplines that exist in universities can be drawn upon to great advantage.

On the other hand, there are obviously types of studies that can best be conducted in the national laboratories or similar institutions. Large-scale, long-term animal studies, for example, are best done in such settings.

In closing, I would want once again to thank the committee for the opportunity to testify. I would be happy to answer any questions.

[The prepared statement of Dr. Upton follows:]

My name is Arthur C. Upton. I am Professor of Environmental Medicine and Director of the Institute of Environmental Medicine, at New York University Medical Center. During the past 30 years, I have devoted much of my professional career to the study of radiation injury, with particular reference to the biomedical effects of low-level irradiation.

Although the biological effects of ionizing radiation have been studied more thoroughly than those of any other physical or chemical agent, our understanding of such effects is still limited. As a result, there remains uncertainty about the magnitude of the risks that may be associated with low-level irradiation. Because the uses of radiation and radiation-emitting devices in the modern world are expanding, there is need to improve our knowledge of any associated risks to human health. Hence further research into the effects of low-level irradiation is warranted. Such research is also important in advancing our understanding of the nature and mechanisms of biological and disease processes, in general.

As concerns the types and levels of research effort needed to address the health hazards of low-level irradiation, I can add little to the conclusions presented in reports by the Comptroller General (Problems in Assessing the Cancer Risks of Low-Level Radiation Exposure, U.S., General Accounting Office, 1981), the Department of Health and Human services (Federal Strategy for Research into the Biological Effects of Ionizing Radiation. Responding to the Congressional Mandate under the Biological Research Extension Act of 1978. P.L. 95-622. NIH

Publ. No. 81-2402, Department of Health and Human Services, 1981), and the National Academy of Sciences (Federal Research on the Biological and Health Effects of Ionizing Radiation, National Academy of Sciences, National Research Council, Washington, D.C., 1981). All of these reviews of the subject have concurred in the conclusion that a broad spectrum of investigative approaches will be required to achieve the degree of understanding needed for more confident assessment of the risks in question. Because of the small magnitude of the risks that can be reasonably predicted to result from low-level irradiation at dose rates compatible with current radiation protection standards, epidemiological studies are not likely to be sensitive enough to measure such risks precisely. Hence a combination of approaches, including both epidemiological and laboratory studies, is called for.

Among the epidemiological studies deserving high priority is the continued follow-up of the a-bomb survivors in Hiroshima and Nagasaki. The information about dose-incidence relationships for carcinogenic, mutagenic, and teratogenic effects derived from the study of these populations is uniquely valuable. Reassessment of the dosimetry, now in progress, must be accomplished as effectively as possible, since the dose estimates are critical to interpretation of existing and future health effects data. Continued follow-up of the survivors for another 20-30 years is essential to determine how long the risk of cancer of various types may remain elevated and to what extent it may vary with age at irradiation, especially in those exposed early in life. Further study of the children of the survivors for genetic effects may also be called for if analytic techniques now under development sufficiently improve our ability to detect and measure mutagenic effects.

Other populations deserving study include those which are large enough, have received sufficiently high and well-defined doses, and in whom health effects can be ascertained accurately enough to provide quantitative dose-effect data. Certain subgroups of occupationally exposed persons fall into this category, but the average dose to radiation workers is so low that the follow-up of all such workers is not likely to be scientifically productive, in my opinion. Similarly, the doses to populations from nuclear fallout and natural background radiation are too low, with few exceptions, to provide a basis for fruitful study.

Among the laboratory approaches deserving of support are those that can help to clarify the mechanisms of injury by low-level irradiation, and thus to improve the theoretical basis for estimating risks by extrapolation from observations at higher doses. Such laboratory approaches should be pursued whenever promising scientific leads and opportunities present themselves. Research areas of timely interest, in addition to those that relate directly to the mechanisms of radiation mutagenesis, carcinogenesis, and teratogenesis, include such questions as 1) the degree to which susceptibility may vary with genetic background, age, sex, physiological condition, organ and cell type, and other variables; 2) the influence of the spatial and temporal distribution of radiation on the dose-effect relationship; 3) the interactive effects of radiation in combination with other physical and chemical agents; and 4) the extent to which differences in radiosensitivity may be modulated through variations in repair and recovery processes.

Because of the sensitivity and accuracy with which doses of radiation can be measured, and because of the wealth of existing knowledge of the biological effects of radiation in humans and other species, further investigation of the health effects of low-level irradiation can be expected to be highly productive, both in extending our capability for risk assessment and in advancing our understanding of fundamental mechanisms involved in gene mutation, gene regulation, cell growth, cell differentiation, cancer, and aging.

To exploit optimally the research opportunities in this subject area will require approaches at virtually every level of biological organization, including both basic and applied investigations. In the national program of research on radiation effects, university-based studies have an important contribution to make, as do studies based in national laboratories and other institutions. In the interest of maximizing the cost-effectiveness of activities in the area, the coordinating efforts of the Interagency Radiation Research Committee are of potential value.

In conclusion, I would like to express my appreciation for the priviledge of expressing my views on this important subject. The contributions made by U.S. research programs to the knowledge of the health effects of low-level radiation are unsurpassed. These programs can be expected to remain productive and to help us cope effectively with radiation risks if given the sustained support they deserve.

Mr. **Gore**. Thank you very much.

We would like to hear next from Dr. William Brandom.

If you can summarize we would appreciate it.

Dr. **Brandom**. What do you want, 2 minutes, 5 or 8?

Mr. **Gore**. Whatever you think is appropriate.

Dr. **Brandom**. Well, it was 10 minutes at first, then 7, or 5, and I got between my prepared summary and a more-inclusive-statement.

Mr. **Gore**. I will let you calculate both the point of diminishing returns and the appropriate time frame. You proceed.

Dr. **Brandom**. As a member of the Futures Panel I say a quote recently in Time attributed to Niels Bohr—"Prediction is very difficult, especially regarding the future." That certainly holds true in this matter.

I am a professor of biological sciences at the University of Denver and my earlier basic research was on the role of chromosomes and embryonic development. Upon moving to the University of Denver a dozen years ago, I was requested to study chromosomes of blood cells of uranium miners and plutonium workers.

The results of those studies were that the frequencies of chromosome changes were observed across subgroups of workers from both of those nuclear-worker populations. Analyses of the data on the plutonium workers revealed that the factors of estimated systemic plutonium burdens and low level external irradiation interacting with age are the main variables accounting for the increase in chromosome aberrations.

The main effects of plutonium burdens are not observed until the workers receive estimates of greater than 50 percent of permissible systemic burden and, more notably, after exceeding estimates of greater than 100 percent of permissible lung burden. I am happy to say that there are very few workers in the highest category at a plant with a workforce of over 4,000.

These and other chromosome studies have been supported by the American Cancer Society, the U.S. Public Health Service, the EPA, NRC, and the Department of Energy and its predecessors.

Although it is not pertinent to my testimony, and it is late in the day, I would like to take this opportunity to publicly thank the legislators and officials in the agencies cited that have had the foresight to provide the resources to conduct research on the biomedical effects of exposures to selected populations exposed to low levels of ionizing radiation.

Regarding the first discussion question for this panel, I have stated in my written testimony that a number of factors influence the answer to the question of what realistically can be accomplished at low doses of radiation. Some of the factors that I cited were the quality of the radiation, dose rate, genetic heterogeneity, and differences in sensitivity in humans, and the difficulty of obtaining good background information by subjects' recall in the case of retrospective studies. The latter makes it difficult to distinguish between effects due to chemical and radiation exposures during the individual's lifetime and any add-on effects from occupation exposure.

I gave the written opinion that any biomedical studies on low level effects will require long periods of time, timeframes greater than is often the case, especially with high dose studies. If long-term research support is not provided, then I think biomedical studies of low levels of ionizing radiation should be reconsidered.

To the second discussion question: "Should future emphasis be placed on biomedical surveillance studies," I have suggested that out of over 100 bioassays developed primarily to test for chemical effects but also for radiation effects, perhaps 8 should begin to be applied, at least in pilot studies, to selected subsets of populations, for example, nuclear workers. The proposed tests would be done by relative noninvasive means, the taking of urine or blood cell samples. This is very important. I think we should be sensitive to the fact that we would be looking at healthy worker volunteers.

Considering the lateness of the hour, I can cut down on my verbal testimony by not recounting in detail the eight tests that I propose that we should consider for biomedical surveillance. Permit me to reiterate them without amplification.

I recommend that we look for the qualitative evidence of possible exposure to toxic substances, by using high performance liquid chromatography assays of urine metabolites; and, follow that up with the Ames salmonella microbiological test on preparations from the other half of the same urine sample. This would be a qualitative biological test for toxic exposures.

The next two tests would attempt to assay for changes in cell function using two immunobiological assays, namely, the T-cell lymphocyte rosette inhibition test and cell-mediated immunity tests. To repeat, these are tests for cell function changes.

The next pair of assays I recommend for biomedical monitoring are unscheduled DNA synthesis and a gene mutation test on blood cells at a particular enzyme locus. These comprise gene function assays.

And lastly, at the organelle level, more specifically the chromosome level, a sister-chromatid exchange test that is used for a vitro chromosome studies of chemical effects; and, the most extensively studied biomedical endpoint at this cellular level, chromosome structural aberrations of cytogenetics.

Some of these assays might prove ineffective because they are at various stages of development and might be dropped or replaced with other developing assays. They could be more effective if applied to selected individuals in populations with relatively high exposures to known or suspected carcinogens.

It would be especially important that: (1) control data bases be developed concurrently; (2) the analysis be done blind or double blind; (3) the simple size be sufficient to provide statistical power, at least in terms of the number of cells; and, (4) that the statistical analysis be appropriate for the data derived.

To the final discussion question concerning university involvement in studies of low level toxic effects, I can shorten this because it would seem self-serving coming from a university professional, but I conclude that university involvement should not be excluded in biomedical radiation studies because: (1) they are generally cost-effective; (2) they are often regionally closest to populations that are of interest; (3) they are partially immune to accusations of conflict of interest; and, (4) the education of future scientists and technologists will in part be, as I said in my more extended written statement, from sectors of the biomedical research community other than universities but mostly limited to the technical and postdoctoral levels. It is, however, the universities that are the primary institutions that provide the baccalaurate, masters, and doctorate professionals currently and in the future. We should not mortgage the future human radiation research resources and if we do, the effects will not be quickly or economically redressed at some later date.

Dr. Upton has already cited the several pertinent Federal agency-generated reports on these issues and the many recommendations contained in them; and I am sure that you and/or your staff are familiar with these reports. I would commend to you, although it is not without some cost, the report on "Guidelines for Studies of Human Populations Exposed to Mutagenic and Reproductive Hazards" (March of Dimes Birth Defects Foundation, White Plains, N.Y.). This report is a response from the scientific community, and contains three sections; cytogenetics, reproductive hazards and mutagenesis; and, I relied very heavily on this report for my statement. However, any suggestions I have made, I take sole responsibility for. I am sure that there are colleagues that were participants in that conference who would not agree that all of these tests are ready to be applied. In that sense, I have not spoken on behalf of the experimentalists today, those whose research is on animals and cell systems from microbes to Rhesus monkeys. I am glad that Dr. Upton addressed that area.

I want to thank you very much for the invitation to be on this panel. In my written testimony I quoted a distinguished scientist in which he pleaded for no more committee reports on low-level radiation effects. I need not repeat that statement, nor do I agree with it. In fact, I think this committee has done a service to go beyond the federally sponsored reports, and to have this hearing including future research plans for low-level radiation effects.

[The prepared statement of Dr. Brandom follows:]

TESTIMONY OF

WILLIAM F. BRANDOM

BEFORE THE

HOUSE COMMITTEE ON SCIENCE AND TECHNOLOGY
SUBCOMMITTEE ON INVESTIGATIONS AND OVERSIGHT

MAY 19, 1982

PANEL 3 - FUTURE EFFORTS

BACKGROUND OF THE WITNESS

An abstract of my biography was submitted to the Subcommittee so I will not recount the details. It is, however, perhaps pertinent to point out my specialty and the milileu in which I do my research. My graduate education was in the cell genetics of the development of lower vertebrates, that is, the role of chromosomes on embryonic development. In 1968, kismet brought me to the University of Denver, situated in a region rich in uranium and facilities for exploiting this energy source - mines, mills, and a plutonium fabrication facility. An administrator at the National Institute for Environmental Health Sciences inquired concerning my possible interest in research on the chromosomes of uranium miners, a population of workers experiencing an epidemic of lung cancer, a consequence of cigarette smoking and underground exposure to ionizing radiation. The results of the uranium miner chromosome study subsequently elicited interest from administrators at the Rocky Flats plutonium fabrication facility in Golden, Colorado for a study of the chromosomes of blood cells of workers at that installation. This long-term study is now entering the tenth year. These and other chromosome (cytogenetic) studies have been supported by the American Cancer Society, the U.S.

Public Health Service, Environmental Protection Agency, Nuclear Regulatory Commission, and the Department of Energy and its predecessors. I would like to take this opportunity to publicly thank the legislators and officials in the the agencies cited that had the foresight to provide the resources to conduct research on biomedical effects of exposures to low levels of ionizing radiation.

The charge to Panel 3 of this hearing is to discuss "Future Efforts". My response to the three discussion topics will be largely confined to what I construe as some research efforts that I believe should be made.

1. WHAT CAN REALISTICALLY BE ACCOMPLISHED THAT IS OF SCIENTIFIC MERIT AT LOW DOSES OF RADIATION?

My perspective on this is to rephrase the question from that provided and to consider the dose range of 1 to 5 rem (Roentgen-equivilant-man, a measure of absorbed radiation). This dose range is selected (although some would consider any dose below 10 or 20 rem as "low") because it is within the range that certainly can be construed as low-level and to which humans are exposed with some frequency from diagnostic procedures or in nuclear-worker settings. The detection of effects by biomedical tests within this exposure range is very difficult, the results and interpretations are controversial, and, if observed, the samples and data are obtained through considerable effort. In fact, Dr. Lauriston Taylor (Past-president of the U.S. National Council on Radiation Protection) has pleaded that "we cease the seemingly endless procession of studies, committees, and hearings on the problem of low level ionizing radiation ..." His position was that, in part, at low levels of radiation, a full and final solution to a dose-effect is not attainable with current capabilities; and, in his view, the effects, if they exist at all, are miniscule. He pointed out that the option was to theorize or postulate a dose-effect relationship at low doses based on extrapolations from high-dose effects. The problem is that the theoretical estimates of effects are sometimes treated as if they were experimentally established facts. This has lead to very imaginative statements as to what may be happening at low doses. As a participant in 3 of the 4 reports cited at the end of this testimony, I am pleased that this House Subcommitte has gone a step beyond the report recommendations and is holding this discussion on Future Efforts.

There are several factors that influence the answer to the question as to what can realistically be accomplished and I shall note just a few.

a) Radiation Quality - Radiations differ in their penetrability and the amount of energy transferred to materials, tissues, or cells. For example, X- and gamma-rays give up relatively scant energy but have high penetration. Neutrons have less penetration but transfer more energy to cells or tissues. Alpha particles have very low penetration but release high energy because of their mass. The relative biological effectivenesss of neutrons and alpha particles are much greater than X- or gamma-rays (neutrons 8X or alpha particles 10-20X). Studies of the effects of acute doses at 5 rem are realistic and have scientific merit. Using the frequencies of blood cell chromosome aberrations as a biomedical endpoint, some laboratories observe a biological response to X- or gamma-rays at 5 rem. Furthermore, studies of individuals in populations chronically exposed for years on an annual basis and within this dose range shown a cumulative effect on chromosome aberrations. (e.g.,nuclear dockyard workers, uranium miners, and plutonium workers). Whether other biological assays currenly under development will prove to be sensitive at these low-dose levels is problematic but should be explored.

b) The Rate at which the Dose is Delivered - Dose rate and dose fractionation very much affect the likelihood of detection of an effect. Five rem received in a very short period of time (acutely) is detectable cytogenetically; the same total dose received in small increments over months or years may not be detected with this assay. However, as noted above, consistent exposures received on an annual basis are detectable and show cumulative effects, at least on one cell system (peripheral blood lymphocytes). The reduction of deleterious effects by dose fractionation, as used in radiotherapy, is due to cellular repair during the intervals between irradiation.

c) Heterogeneity in Response - Humans are, excepting monozygotic twins, phenotypically (by appearance) and genotypically (genetic endowment) very heterogeneous. Studies of cells of individuals with certain genetic diseases reveal that they are much more radiosensitive than those without the diseases. Thus, within the human population we might expect that there is a spectrum of radiosensitivity with some more likely to be sensitive to low-level irradiation than others. This is likely to affect any biomedical studies. The corollary of this is that, especially at low doses, an adequate population of individuals and cell samples must be obtained in order to cover the spectrum of sensitivities.

d) Adequate Background Information - Complete background information (demographic, medical history, personal habits, age, sex, occupations, etc.) must be obtained so as to be aware of confounding and perhaps interacting effects from a variety of chemicals and radiations not connected with the add-on low-level radiation effects being studied. In this sense, biomedical studies share difficulties in common with retrospective epidemiologic studies.

In spite of these and other confounding factors, it seems to me that if we do not carry out low-level radiation studies, we may never come closer to an understanding of this problem. Because of the low frequency of events at the low exposure levels, it is imperative that long-range, studies of chronic exposure be done. In an atmosphere of "more bang for the Buck", this is, with few exceptions, not the usual way of supporting research; however, I believe it is essential to any potential success for low-level radiobiological studies. In short, there is no way to obtain quick answers.

2) SHOULD FUTURE EMPHASIS BE PLACED ON BETTER MEDICAL SURVEILLANCE AND BIOMEDICAL STUDIES?

Prospective or retrospective surveillance of individuals within selected groups known to be exposed to toxic physical or chemical agents should be monitored by clinical and biomedical assays; and, if indicated, with epidemiological studies. Of the more than 100 bioassays developed to test for mutations or carcinogenesis, less than a dozen currently offer promise for application for in vivo effect studies in humans. Though there is some disagreement among scientists concerning the applicability of specific assays, most agree that a tier of assays should be used, especially for in vitro testing of chemicals known or suspected to be mutagens. Future studies should use a battery of assays as a check for false-negatives or false-positives and should include different levels of chemical and biological organization testing. In addition, subject selection for in vivo human studies must take into account the progressive exposure to low levels of toxic substances during their lifetimes. People are exposed to low-level background radiations from cosmic, terrestrial, and man-made sources (e.g., weapons fall-out, building materials, and diagnostic or therapeutic radiation). Chemical exposures are experienced through personal habits, food additives, therapeutic or "recreational" drugs, and technologically-enhanced chemical pollutants in industrialized settings. This litany of sources of exposure is not meant to instill undue concern nor does it represent my support of overly stringent regulations for environmental pollutants. I share with many the distaste for the pronouncements of the "carcinogen-of-the-week", fearing that music is rapidly moving up the list. The purpose of my listing is to point out that it will be exceedingly difficult to differentiate between the effects of background, low-level exposures and those incurred as a consequence of add-on, low-level diagnostic or therapeutic agents, industrial pollutants, or occupational exposures. Additionally, individual differences in responses are expected because of the previously mentioned genetic heterogeneity of humans. As a paradigm of what I think might or should be done, I proposed, at a recent international conference on radiation hazards in mining, that we attempt to identify the exceptionally sensitive uranium miners using a tier of tests on urine and white blood cells. Uranium miners are exposed to radioactive radon daughters, gamma rays from the uranium ore, uranium ore dust, and diesel fumes. Therefore, any detectable additional biomedical effects after entering the mining environment could be the consequence of a combination of chemical and radiation pollutants in the workplace. Chemical or biological assays might be capable of detecting the interactive effects of add-on occupational pollutants.

The first assays proposed were to test for exposures by an analytical chemical method (high performance liquid chromatography) for metabolites in urine; and, biologically by a microbial mutagen test of urine metabolites (the Ames Salmonella test). These assays for exposure would then be followed up with tests for changes in cell function using radio- and chemo-sensitive blood cells. Two immunobiological response tests (T-cell lymphocyte rosette inhibition and cell-mediated immunity tests) hold some promise for evidence of changes in cell function. In the third tier of tests, one assays for

DNA repair as a consequence of toxic insult and another tests for a specific gene mutation (the HGPRT locus). The last tier, testing for changes at the subcellular organelle level, are cytogenetic tests which would be done on the same blood cell sample used in the prior assays. The sister-chromatid-exchange test is an assay for chemical effects at the chromosome level. The frequency of chromosome breaks and rearrangements (structural aberrations) assays for radiobiological effects. To recapitulate, and using the uranium miners as an example, there are bioassays (at various stages of development) that can be used for selected populations in concert with clinical tests and/or epidemiologic studies. Although populations likely-at-risk would more efficiently be studied if high doses of potent mutagens or carcinogens are suspected, low-dose populations should also be studied if bioassays sufficiently sensitive are to be identified and the uncertainties of extrapolations from high to low doses clarified. It is especially important that: i) carefully selected control subjects be used to provide an adequate control data base; ii) the assays be done and the analyses run in a manner that precludes knowledge of the subjects' identification; iii) that the sample size be sufficient to provide statistical power; and, iv) that the statistical analyses be appropriate to the derived data. If these and other caveats are adhered to, some emphasis for these kinds of studies are recommended for selected populations receiving low-level exposures to radiation and radiation plus chemicals.

3. IS THERE A NEED FOR MORE UNIVERSITY INVOLVEMENT IN SUCH STUDIES?

Although it may appear to be self-serving, I believe the answer to this question is certainly yes; but there are many resources for research. There are non-profit and profit-making institutes, in-house industrial environmental health units, in-house federal (and to a much lesser extent state) laboratories, and the universities. Without in any way meaning to disparage the capabilities of non-university sources to conduct highly skilled research on radiation or chemical effects, indeed, these are powerful resources with very skilled professionals, there would appear to be several reasons why universities and university laboratories should be involved in such studies.

Even with the current negotiations, re-evaluation, and changes in computing indirect cost rates for universities, they generally have proven cost-effective. There are probably several reasons for this: i) in most instances the professionals, staff, and students are paid less and the fringe benefits cost less when compared with the other research sectors; ii) they are non-profit institutions; and, iii) they have additional support structures - tuition, alumni and non-alumni donations, and so forth.

I will not attempt to justify support for university research based on the diversity of professional talents across university disciplines because in specific problem-focused areas, non-university research resources often have impressive capabilities. There are, however, situations wherein universities or inter-university cooperationin the study of a particular regional reseach problem proves very effective.

With some reluctance, I suggest that there is a non-scientific reason for university involvement in research on the biomedical effects of radiation or chemicals. Assuming competency for university personnel to do the research and to objectively interpret the findings, in an area as charged with non-scientific rhetoric as are radiation effects (or non-effects), university personnel are less subject to the accusation of complicity in "cover-up" statements. This is in no way meant as an aspersion of the motives, scientific integrity or professional skills of non-university professionals. Rather it is an indictment of the distortion of the evidence and issues for radiation effects by a segment of the media that has been known to discount the views of excellent radiation scientists if they happen to be employees of other than a university organization. These patently unfair tactics are to be disparaged, but the reality is that this is one advantage of university research on a socially sensitive subject. I would hasten to add that this should not be given especially great weight in the dialogue as to whether to support university research on this subject.

An obvious, and perhaps the best, reason for support of university radiobiological and other areas of research, is the education of the pre-professional, professional and technical personnel necessary to provide continuity in radiobiology or other research areas. Certainly the non-university research sectors carry out this function at different stages, especially at the post-doctoral and technical level; but, it is the universities that are the primary institutions that provide the baccalaureate, masters, and doctorate professionals currently and for the future. If the resources for the university research community are not forthcoming we will mortgage the future human research resources and the effects will not be quickly and economically redressed at some later date.

SUMMARY

Regarding the first discussion question, which I paraphrased to focus on low-level radiation effects, radiation quality, dose-rate, and other factors affect the results of biomedical studies. Any results will be hard gotten and, because of the low frequency of events, will be difficult to interpret. Evidence for effects at low yearly doses accumulated over years is that a response to estimated doses or radiation burdens is observed (the cytogenetics of nuclear dockyard workers, uranium miners, and plutonium workers).

To the second discussion question, I suggested that medical surveillance and chemical and biological assays should be done on carefully selected populations exposed to low-levels of ionizing radiation and chemicals. I proposed a battery of tests and recognize that some of theassays are still in development but hold out the promise of the detection of individuals that might be especially sensitive to toxic physical and chemical agents. Several caveats were cited to optimize the potential for success using the assays.

To the final discussion question concerning university involvement in studies of low-level toxic effects, I opined that university involvement should not be excluded because: i) they are generally cost-effective; ii) they are often regionally closest to populations that are of interest; iii) they are partially immune to accusations of conflict-of-interest; and, iv) the education of future scientists and technologists will be thwarted if universities do not adequately share in these studies.

I have studiously avoided as much technical jargon and obfuscation as possible. Though this is fraught with the peril of not being much more than a series of opinions, I erred on that side in an attempt to to state my position. To partly correct for my slight of technical statements or citations, I commend to you a few reports, some or all of which you or your staffs may have read. Three of the four are government sponsored and the fourth sponsored in part by the government.

SELECTED REPORTS

Federal Research on the Biological and Health Effects of Ionizing Radiation, National Research Council, (Two volumes, the second appendices), National Academy Press, Washington, D.C., 1981.

Guidelines for Studies of Human Populations Exposed to Mutagenic and Reproductive Hazards, (Arthur D. Bloom, Ed.), Proceedings of Conference held January 26-27, 1981, March of Dimes Birth Defects Foundation, White Plains, N.Y., 1981.

Report of the Interagency Task Force on the Health Effects of Ionizing Radiation, Office of the Secretary, U.S. Department of Health, Education, and Welfare. Washington, D.C., 1979.

Review of the Department of Energy Research on Human Health Effects of Low Doses of Ionizing Radiation, Division of Medical Sciences, Assembly of Life Sciences, Nationa Research Council, National Academy of Sciences, Washington, D.C., 1980.

Vita

William F. Brandom, Ph.D.
Professor, Biological Sciences
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Education

A.B. Biological Sciences, Stanford University, 1951
M.A. Biological Sciences, Stanford University, 1954
Ph.D. Biological Sciences, Stanford University, 1958
Postdoctoral Fellowship, NIH, NCI, Princeton University, 1958-59
Postdoctoral Fellowship, NIH, NICHH, St. Andrews University, 1966

Professional Positions

1959-1960	Tulane University, Department of Biology, Instructor
1960-1965	Tulane University, Department of Biology, Assistant Professor
1965-1967	Tulane University, Department of Pathology, School of Medicine, Research Professor
1967-1968	Delta Regional Primate Research Center, Visiting Research Scientist
1968-1972	University of Denver, Department of Biological Sciences, Associate Professor (Tenure conferred, Fall, 1971)
1972-	University of Denver, Department of Biological Sciences, Professor .

Accomplishments (Honors, Awards, Grants)

Eli Lilly Scholarship, Stanford University
University Honors Fellowship, Stanford University
NSF Research Participation Grant, 1971, $ 9,270.
HEW, PHS, FDA, BRH, Grant, 1971, $ 52,295.
NSF Research Participation Grant, 1972, $ 12,440.
HEW, PHS, FDA, BRH, Grant, 1972, $ 38,929.
AEC (Dow Chemical), 1972, $ 13,226.
U.S. Nat. Acad. Scs. Scientist Exchange to Eastern Europe, 1973.
HEW, PHS, FDA, BRH, Grant, 1973, $ 29,921.
AEC (Dow Chemical), 1973, $ 12,152.
AEC (Dow Chemical), 1974, $ 39,984.
AEC (Dow Chemical), 1975, $ 55,664.
ERDA, DBER, Contract No. E(29-2)-3639, 1976, $115,000.
ERDA, DBER, Contract E(29-2)-3639, 1977, $143,750.
DOE, DBER, Contract ALO-EY-76-S-04-3639, 1978, $138,038.
DOE, DBER, Contract ALO-De-AS04-76EV-03639, 1979, $139,966.
CDH, Contract C295431, 1979, $15,000.
DOE, HHAD, OHER, Contract ALO-DE-AS-04-76-EV-03639, 1980, $166,000.
(Included $33,000 for Biomedical Mobile Laboratory)
EPA/CDH, Contract C296310, 1980, $44,481.
DOE, HHAD, OHER, Contract ALO-DE-AS-04-76-EV-03639, 1981, $130,000.
NRC/CDH Contract C297367, 1981, $24,000.
DOE, HHAD, OHER, Contract ALO-DE-AS-04-76-EV-03639, 1982, $ 65,000.
(TERMINAL YEAR)

Mr. GORE. Thank you very much, I appreciate that.

We will consider this for inclusion in the record, if that is okay. What is that report that you cited? The first one?—the second one in your list? That will be fine.

Dr. Halperin.

Dr. HALPERIN. My name is Dr. William Halperin, I am Chief of the the Industrywide Studies Branch of the Division of Surveillance, Hazard Evaluations and Field Studies of the National Institute for Occupational Safety and Health [NIOSH], a component of the Centers for Disease Control [CDC]. I am a physician and an epidemiologist.

I received a Masters of Public Health and a Medical Degree from Harvard in 1971 and 1973. I trained in internal medicine at Harvard from 1973 through 1975. I then joined the CDC's Epidemic Intelligence Service, and after completing a preventive medicine residency, I moved to NIOSH in 1978.

The Industrywide Studies Branch of NIOSH, which I head, draws on occupational physicians, epidemiologists, and industrial hygienists to conduct a variety of medical and epidemiologic studies. Several of these studies concern worker exposure to radioactive elements. It is from the perspective of a generalist without specialized training in radiation but with responsibility for several pertinent studies on health effects of the workplace that I address this subcommittee.

Prevention of occupational disease depends on a continuum of preventive practices. The first means of prevention of occupational disease is the premarket testing of industrial agents before they enter commerce in order to identify a hazard before workers are exposed. Laboratory animals and other test systems such as the Ames Test are used to evaluate new chemicals before they are used in industry.

Premarket testing is mandated by the Toxic Substances Control Act [TOSCA]. The second means of prevention is substitution of hazardous agents with nonhazardous alternates. An example might be the replacement of asbestos in many commercial products. Asbestos, which causes lung cancer and lung disease, can often be replaced with insulating materials that have been shown to be less toxic. When hazardous agents must be present, we then depend on adequate engineering design of process so that exposure is limited to levels regulated by the Occupational Safety and Health Administration [OSHA] or recommended by voluntary groups such as the American Conference of Governmental Industrial Hygienists [ACGIH].

Industrial hygienists, whether working for companies, unions, or government, test or monitor the workplace environment for hazardous agents. Environmental monitoring is used to insure the effectiveness of engineering controls already in place and to target parts of the workplace that need improved control of hazardous agents. We can sometimes measure the level of hazardous agents in the blood or urine of workers as another gauge of the adequacy of the control of exposure.

In addition, we can screen or medically examine workers for disease with the aim of detecting disease in an earlier and more treatable stage, or to use in combination with exposure information to pinpoint risky chemicals or processes.

As a further measure of defining occupational illness, we can analyze data such as death certificates, in order to gauge the long-term health consequences of occupational exposures.

The committee's question to me is whether research in any or all of the epidemiologic modalities would be valuable at current levels of exposure to radioactive agents.

I will draw on current activities at NIOSH to exemplify how a spectrum of studies could be useful. We recently studied kidney damage in uranium processors. Our study cost less than $20,000 and one person-year of professional time. We studied 39 workers at a uranium mill who grind uranium ore and process it to yellow cake, a complex mixture of uranium diuranates, which is a feedstock for uranium enrichment plants. We aimed our study at detecting kidney damage because the current standard for uranium exposure is based on the presumption that the kidney is the most sensitive organ affected by uranium exposure.

Prior to 1979, when a new uranium mill was constructed, records show that the levels of uranium content of the workers' urine were frequently above permissible levels. In a field study conducted at the plantsite, we collected samples of blood and urine and took personal medical histories. Rather than just study protein in the urine, we looked at beta-2-microglobulin, a small protein. Beta-2-microglobulin leaks from the kidneys of workers exposed to some heavy metals.

In addition, we looked for leakage of amino acids, the small building blocks of protein. We believe our results, which I stress do need confirmation in another mill, suggest that by using this sensitive marker of kidney damage not now being used in uranium workers, that the uranium mill workers' kidneys have sustained some damage. Prior to this small study, there never had been an occupational survey of uranium exposed workers using modern, sensitive indicators of kidney damage.

This survey should stimulate two types of research. First, we should reassess the methods now in use to test for kidney damage in uranium workers. Second, we should ask how common it is that workers in our nuclear industries have tests like the urine test for uranium that show that they have more than accepted levels of exposure to radioactive elements. To draw a parallel from the control of infectious diseases, in an effort to control polio, our efforts must be divided between developing an adequate vaccine and insuring its use.

To prevent occupational disease, we must not only try to gauge a safe standard by doing research, but also we must adequately monitor the workplace to insure that exposures are being kept within the established levels of safety.

The next two paragraphs concern the possibility of using chromosomal analysis in occupational studies, but I think I will defer those and enter them in the record.

In describing several medical epidemiologic approaches to studying workers exposed to nuclear agents, I do not by any means wish to minimize the value of classical epidemiologic studies or mortality. These studies have been exceptionally successful in the past.

For instance, beginning in 1952 NIOSH and its predecessor agencies have studied the mortality experience of thousands of uranium miners exposed in the mines to radioactive agents known as radon daughters.

Radon daughters are the radioactive disintegration products of radon gas. Our studies have shown uranium miners exposed to radon daughters to be at five times excess risk of lung cancer. This type of mortality study, if well designed and conducted, is a keystone to our understanding the risks of radiation.

For instance, there is a real possibility that a mortality study of uranium miners who in the past were exposed to what is now the current permissible exposure standard would shed considerable light on the adequacy of this standard. NIOSH is currently reexamining the data we now have on this population to see if such a study is feasible.

In summary, I hope that I have presented a range of possibilities for potential occupational studies in the radiation field. These investigations could range from epidemiologic studies of mortality, through medical epidemiologic studies of pathology such as kidney damage and abnormal chromosomes, to studies of engineering controls such as those which could be designed in ventilation systems. In essence, the choice of a particular study depends on its feasibility and on its potential payoff in preventing ill health.

Thank you. I will be pleased to respond to any questions you may have.

[The testimony of Dr. Halperin follows:]

DEPARTMENT OF HEALTH & HUMAN SERVICES Office of the Secretary

Washington, D.C. 20201

STATEMENT ON

LOW LEVEL IONIZING RADIATION

BY

WILLIAM E. HALPERIN, M.D., M.P.H.

NATIONAL INSTITUTE FOR OCCUPATIONAL SAFETY AND HEALTH
CENTERS FOR DISEASE CONTROL
DEPARTMENT OF HEALTH AND HUMAN SERVICES

BEFORE

THE SUBCOMMITTEE ON INVESTIGATIONS AND OVERSIGHT

COMMITTEE ON SCIENCE AND TECHNOLOGY

U.S. HOUSE OF REPRESENTATIVES

May 19, 1982

My name is Dr. William Halperin. I am Chief of the Industrywide Studies Branch of the Division of Surveillance, Hazard Evaluations and Field Studies of the National Institute for Occupational Safety and Health (NIOSH), a component of the Centers for Disease Control (CDC). I am a physician and an epidemiologist. I received a Masters of Public Health and a Medical Degree from Harvard in 1971 and 1973. I trained in internal medicine at Harvard from 1973 through 1975. I then joined the CDC's Epidemic Intelligence Service, and after completing a preventive medicine residency, I moved to NIOSH in 1978.

The Industrywide Studies Branch of NIOSH, which I head, draws on occupational physicians, epidemiologists, and industrial hygienists to conduct a variety of medical and epidemiologic studies. Several of these studies concern worker exposure to radioactive elements. It is from the perspective of a generalist without specialized training in radiation but with responsibility for several pertinent studies on health effects of the workplace that I address this Subcommittee.

Prevention of occupational disease depends on a continuum of preventive practices. The first means of prevention of occupational disease is the premarket testing of industrial agents before they enter commerce in order to identify a hazard before workers are exposed. Laboratory animals and other test systems such as the Ames Test are used to evaluate new chemicals before they are used in industry. Premarket testing is mandated by the Toxic Substances Control Act (TOSCA). The second means of prevention is substitution of hazardous agents with nonhazardous alternates. An example might be the replacement of asbestos in many commercial products. Asbestos which causes lung cancer and lung disease can often be replaced with another insulating material that has been shown to be less toxic. When hazardous agents must be present, we then depend on adequate engineering design of process so that exposure is limited to levels regulated by the Occupational Safety and Health Administration (OSHA) or recommended by voluntary groups such as the American Conference of Governmental Industrial Hygienists (ACGIH).

Industrial hygienists, whether working for companies, unions, or government, test or monitor the workplace environment for hazardous agents. Environmental monitoring is used to insure the effectiveness of engineering controls already in place and to target parts of the workplace that need improved control of hazardous agents. We can sometimes measure the level of hazardous agents in the blood or urine of the worker as another gauge of the adequacy of the control of exposure. In addition, we can screen or medically examine workers for disease with the aim of detecting disease in an earlier and more treatable stage or to use in combination with exposure information to pinpoint risky chemicals or processes. As a further measure of defining occupational illness, we can analyze data such as death certificates, in order to gauge the long-term health consequences of occupational exposures.

The Committee's question to me is whether research in any or all of the epidemiologic modalities would be valuable at current levels of exposure to radioactive agents.

I will draw on current activities at NIOSH to exemplify how a spectrum of studies could be useful. We recently studied kidney damage in uranium processors. Our study cost less than $20,000 and one person-year of professional time. We studied 39 workers at a uranium mill who grind uranium ore and process it to yellow cake, a complex mixture of uranium diuranates, which is a feedstock for uranium enrichment plants. We aimed our study at detecting kidney damage because the current standard for uranium exposure is based on the presumption that the kidney is the most sensitive organ affected by uranium exposure. Prior to 1979, when a new uranium mill was constructed, records show that the levels of uranium content of the workers' urine were frequently above permissible levels. In a field study conducted at the plant site, we collected samples of blood and urine and took personal medical histories. Rather than just study protein in the urine, we looked at beta-2-microglobulin, a small protein. Beta-2-microglobulin leaks from the kidneys of workers exposed to some heavy metals. In addition, we looked for leakage of amino acids, the small building blocks of protein. We believe our results, which I stress do need confirmation in another mill, suggest that by using this sensitive marker of kidney damage not now being used in uranium workers, that the uranium mill workers' kidneys have sustained some damage. Prior to this small study there never had been an occupational survey of uranium exposed workers using modern, sensitive indicators of kidney damage.

This survey should stimulate two types of research. First, we should reassess the methods now in use to test for kidney damage in uranium workers. Secondly, we should ask how common it is that workers in our nuclear industries have tests like the urine test for uranium that show that they have more than accepted levels of exposure to radioactive elements. To draw a parallel from the control of infectious diseases, in an effort to control polio our efforts must be divided between developing an adequate vaccine and insuring its use. To prevent occupational disease we must not only try to gauge a safe standard by doing research, but also we must adequately monitor the workplace to insure that exposures are being kept within the established levels of safety.

Another type of experimental test that offers potential is chromosomal analysis. To do this kind of research blood samples are collected and cultured. Chromosomes or the genetic material from cells are examined in detail to identify ones that are broken. Several populations with excess risk of cancer, such as benzene-exposed workers, have been shown to have excess levels of broken chromosomes in blood cells. Even though chromosomal breakage does not tell us the disease future for the individual, a workforce with increased genetic damage may be at increased risk for occurrence of cancer. Cancer and chromosomal damage both reflect the adverse biologic activity of radiation. If we could control occupational chemical or radiation exposure, so as to minimize or eliminate chromosomal damage, the possibility of cancer occurring should probably be decreased as well.

In essence chromosomal studies should be evaluated as a means to assess the adequacy of current radiation standards. NIOSH has proposed a chromosomal study in a nuclear shipyard. This proposal is currently being reviewed by the National Academy of Sciences (NAS). Several hundred workers would be involved in donating blood samples. I stress that a chromosomal study presupposes that a radiation or chemical hazard that causes genetic damage also could cause increased cancer risks, and that control of radiation exposure to levels with minimal genetic damage could possibly reduce cancer risk.

In describing several medical epidemiologic approaches to studying workers exposed to nuclear agents I do not by any means wish to minimize the value of classical epidemiologic studies of mortality. These studies have been exceptionally successful in the past. For instance, beginning in 1952 NIOSH and its predecessor agencies have studied the mortality experience of thousands of uranium miners exposed in the mines to radioactive agents known as radon daughters. Radon daughters are the radioactive disintegration products of radon gas. Our studies have shown uranium miners exposed to radon daughter to be at five times excess risk of lung cancer. This type of mortality study, if well designed and conducted, is a keystone to our understanding the risks of radiation. For instance, there is a real possibility that a mortality study of uranium miners who in the past were exposed to what is now the current permissible exposure standard would shed considerable light on the adequacy of this standard. NIOSH is currently reexamining the data we now have on this population to see if such a study is feasible.

In summary, I hope that I have presented a range of possibilities for potential occupational studies in the radiation field. These investigations could range from epidemiologic studies of mortality, through medical epidemiologic studies of pathology such as kidney damage and abnormal chromosomes, to studies of engineering controls such as those which could be designed in ventilation systems. In essence, the choice of a particular study depends on its feasibility and on its potential payoff in preventing ill health.

Thank you. I will be pleased to respond to any questions you may have.

Mr. GORE. Thank you very much.

Dr. Brandom, the tests that you mentioned included your analysis to detect chemicals in the urine, test for changes in blood cells and in cellular DNA and to test for abnormality in chromosomes.

Has such tier testing been attempted?

Dr. BRANDOM. Mr. Chairman, it has been highly recommended by genetic toxicologists that a tier of tests be done. These scientists are especially addressing themselves to the question of chemical toxicology.

I am pleased to hear today, to have it repeated again and again that it is not only low levels of ionizing radiation that we must be concerned about, but the interaction of radiation and chemicals. As far as tier tests applied to human body fluids and cells as a biological monitor, it is my idea, and if it is a bad one, I am solely responsible. As for the high performance liquid chromatography test, for example, yes, it is used in forensic medicine, applied for the analysis of various metabolites of drugs for obvious reasons, for metabolites in the urine of smokers, and so forth.

The salmonella microbiological test has been done in vitro on thousands of chemicals, and in some instances on urine samples. You've already heard about cytogenetics tests done on humans exposed to occupational irradiation. As for a combination of a tier of tests such as I have recommended, some people would think some of these tests are premature for in vivo studies, and, no, they have not been done in this particular battery of tests in concert.

Mr. GORE. Earlier witnesses said this great pool of data concerning U.S. workers exposed to radiation was probably not a goldmine and one would probably not be able to make valuable conclusions about the health effects of low-level radiation.

Would you agree or disagree with that general statement?

Dr. HALPERIN. That depends on the target question that one is addressing. It is I think difficult to answer it either in a total yes or a total no.

For instance, there are sets of data such as the uranium miners data where there is a large accumulation of data that should be mined if one has specific hypotheses in mind, such that the data might be addressed to those specific hypotheses.

The act of collecting the data in a routine fashion only allows one to address specific hypotheses. It in itself does not address those hypotheses. Therefore, whether the data collected by the Department of Energy is a goldmine or not depends on its value in addressing a list of reasonable questions that need answering in order to protect worker health.

Mr. GORE. All right. Very good.

Dr. Upton, the testimony earlier did question the scientific value of the study, but recommended that it continue. You mention a combination of epidemiological and laboratory studies as being called for.

Would you recommend increasing surveillance and decreasing the epidemiologic study of low levels of radiation or the reverse?

Dr. UPTON. Mr. Chairman, I think my position would compare with the position that I understood Drs. Hutchison and Beebe and Mr. Jablon recommended, that the likelihood of designating radiation effects in the large cohort of workers is quite small, unless our current risk estimates are grossly in error.

On the other hand, the value of a careful medical surveillance of such a population is indisputable. My statement was not intended to imply that I thought one should subject this poulation to a battery of laboratory-type clinical studies. There may be certain types of clinical investigations which are in fact worth exploring for their ability to provide information in some sense on radiation workers.

Some of these have been mentioned. But this is not an area in which I have expertise.

Mr. GORE. Dr. Marks, you suggest a national radiation workers registry. How well are records kept now?

Dr. MARKS. To the best of my knowledge, there is a system that NRC has and also DOE has certain data but in the past, at least, there has not been a combined complete set of data that would permit one to access by individual accumulative dose that the individual may have gotten in several plants.

So right now, it is not up to the point where it is usable in epidemiologic studies, and I think I would have to defer to Dr. Goldsmith, who is in the audience, for information about where it is going at the present time.

Mr. GORE. Well, if we hold the record open, would you gentlemen be willing to answer additional questions for the record. We certainly appreciate your patience. You have been most understanding.

Again I apologize, thank you very much for your help here today.

Mr. GORE. I would like to now call on our final witness and the most extensive apologies of all go to you, Robert Alvarez, for waiting this long. I certainly appreciate it.

Would you raise your hand.

[Witness sworn.]

Mr. GORE. Thank you very much.

Without objection, the entire text of your statement will be included in full in the record, and if you could, please, summarize, I would appreciate it. I recognize that that puts a burden on you in the sense that your perspective is different from most of the witnesses that have appeared.

STATEMENT OF ROBERT ALVAREZ, WASHINGTON REPRESENTATIVE, ENVIRONMENTAL POLICY CENTER

Mr. ALVAREZ. I will attempt to summarize my statement and not cover areas covered by previous speakers.

My name is Robert Alvarez, a Washington Representative of the Environmental Policy Center, a nonprofit environmental lobbying organization. I appreciate the opportunity to testify before your committee, Mr. Gore, and I commend your work in this area.

I think I will address what we consider to be the fundamental problem in the area of Federal radiation health effects research as it affects the nuclear industry. That is the fact that the nuclear weapons bureaucracy has in essence dominance over this area by funding.

In 1979, the President's Interagency Task Force on Ionizing Radiation determined that the DOE effectively controls over 60 percent of all Federal radiation health effects research. One only has to read the AEC, Atomic Energy Acts of 1946 and 1954 and the Energy Reorganization Act of 1974 to ascertain that the Energy Department is in the business of making nuclear weapons and promoting nuclear energy. The DOE is not a public health agency.

This fundamental conflict of interest has created a record of suppression and distortion of science. It has allowed the exposure of thousands of Americans to nuclear weapons radiation which may now result in significant health damage and enormous financial liability for the Energy Department.

I bring this up because when the Department of Energy does to its planning, it has to include this into the conduct of its research. For example, the total damage claimed by residents living near the Nevada Test Site owned by the Department of 0, the 1983 budget for DOE's nuclear weapons program is approximately $5 billion. In essence two-fifths of the DOE's weapons program is jeopardized if these claims are indeed going to be paid out.

An estimated 250,000 military personnel were involved in open air nuclear weapons detonations, many of these soldiers could have received dangerous exposures.

Swaths of land equalling hundreds of acres surrounding the Rocky Flat nuclear weapons plant near Denver, Colo., the Nevada Test Site, and the Savannah River Plant near Aiken, S.C., are contaminated with plutonium relased from DOE facilities. Preliminary evidence from health surveys of nuclear weapons workers, radioluminizing workers, atomic soldiers, and downwind civilian residents suggest increased human sensitivity to fatal cancer induction from levels of ionizing radiation considered safe by Federal authorities.

As early as 1978, when many of these problems came to light through congressional investigations, the Energy Department had already established a major in-house health effects research program influenced by the impact reductions in occupational exposure limits and compensation claims would have on DOE operations. These research programs fall into two categories: Epidemiological research of DOE and DOD contract employees and dose assessment from nuclear weapons testing.

The Dose Assessment Advisory Group [DAAG], has since met regularly to review the work of these DOE contractors. The purpose of this advisory group is to establish criteria for determining fallout doses. The criteria will be used in filing compensation claims in Federal court and possibly other compensation avenues established by Congress.

Already, contractors for the DAAG study are testifying on behalf of the Government in one of the court cases on fallout damage. Testifying prior to completing the dose assessment placed the credibility of this group in question.

The DOE epidemiology program deserves special attention because of the large number of DOE contract employees exposed to radiation who have reached the end of cancer latency periods. If Hanford, Oak Ridge and Savannah River worker populations were combined in one study, it would rival the sample size of the Japanese atomic bomb survivor studies, the current scientific basis for official risk estimates.

A brief mention about the question of sample size. The speakers previously have asserted that it is relatively impossible to actually observe actual effects at low dose because of the noise. And they have cited a paper by Charles Land which appeared in Science I believe in 1980, 1981.

In looking at that paper, Mr. George Neil, University of Birmingham, wrote a paper which was given to the Nuclear Regulatory Commission in November of 1980. The basic criticism of the Lamb paper is that his model assumes that all cells are homogenous. That does not exist in nature. There are certain cells that are more sensitive to radiation than others. So therefore the mathematical basis of Dr. Lamb's assertion may not be correct.

By the time Congress designated the HHS as the main coordinator of radiation health effects research under Public Law 95-522, the DOE had already funded the most sensitive radiation epidemiology studies.

The contracts for these studies were given out on a sole source basis without the standard competitive bidding, protocol submission, and peer review procedures inherent in Federal public health agency research. Thus, the DOE has taken steps to prevent epidemiological research from developing outside of its control.

For example, in 1974 the DOE decided to terminate funding for a health and mortality study of DOE contract employees directed by Dr. Thomas Mancuso of the University of Pittsburgh. Mancuso had refused to cooperate with DOE officials in downgrading a 1974b study of Hanford workers which suggested excessive cancer mortality among them.

He then later published positive findings on his own in 1977. There have been five more papers to appear in scientific journals this year by Mancuso.

The DOE gave most of Mancuso's research project to Oak Ridge Associated Universities, with the exception of the Hanford study which went to Battelle-Northwest, a major nuclear contractor. The ORAU and Battelle contracts were let without proper protocol or peer review to groups with no significant background in epidemiology. In fact, ORAU received the contract even before it chose a principal investigator.

Dr. Sidney Marks, who directs the Battelle study of the Hanford workers, was Dr. Mancuso's contract officer who terminated his contract. Dr. Ethyl Gilbert, who works under Dr. Marks, produced an analysis for the DOE in 1974 showing excessive cancer deaths among exposed Hanford workers. DOE quickly buried the report. Drs. Marks and Gilbert have never referred to that analysis or explained in any of their written criticisms of the Mancuso study why they do not support its findings.

These contract management practices are not conducted by public health research agencies such as the National Institutes of Health. This Fall, the Interagency Radiation Research Committee, chaired by the NIH, plans to issue recommended criteria for radiation health effects research contract review; these recommendations, we hope, will stop these abuses from occurring in the future.

However, the problem of conflicting interests remains, relative to the most sensitive research areas influencing standard setting, compensation claims, and the future limits of nuclear weapons and nuclear power.

I will summarize briefly the other part of my testimony. I bring to your attention a report and investigation conducted by the Commerce Committee, which looked into a matter concerning radiation fallout from the Nevada Test Site on people and sheep living nearby.

They issued a report in 1980 entitled "The Forgotten Guinea Pigs". They concluded that the Government inexcusably failed to give adequate warning to the sheepmen, knowingly.

Dr. Marks coauthored a sheep study with Dr. Leo Bustad suggesting that radioiodine ingestion by the Utah sheep was too small to have caused significant injury. Dr. Harold Knapp, a radiation expert in DOD, in the 1979 congressional hearings analyzed the Bustad/Marks study and found that "the material which appeared to have been withheld and distorted was the effects of radioiodine in the fallout ingested by pregnant ewes or fetal lambs."

Dr. Lushbaugh, Chairman of ORAU's Medical Division, was commissioned by the AEC to study potential effects of fallout on the wool and skin of sheep. Lushbaugh in his study, "believed that although similarities were found to those (lesions) seen in the Cedar City (Utah) sheep, such lesions were found to be produced by physical and/or infectious agents." He concluded "that radiation was not the cause of death."

An AEC internal report of November, 1953, stating, "no positive evidence was found of an infectious organism that could account for the abnormal losses" of the Utah sheep did not change Lushbaugh's conclusions, which were used in court in 1956. No consensus on the Lushbaugh findings was reached among AEC, State and U.S. Public Health officials. This situation prompted the AEC to fabricate a statement suggesting that all reviewers of the Lushbaugh study agreed with his conclusions.

"The Forgotten Guinea Pigs" states, "By falsely using the October 27th statement, the AEC misrepresented the group's belief * * * and concluded that * * * the lesions were not produced by radioactive fallout."

This congressional investigation resulted in the sheepmen reopening their case against the Government. Here we have past research of two DOE sponsored scientists, who are now in charge of highly sensitive research, criticized by a congressional report and by a Federal pubic health agency, and now subject to litigation involving fraud upon a Federal court. Government credibility can only erode further with this kind of research management.

Mr. GORE. If I could ask you to summarize briefly. I mean no discourtesy. I am supposed to host a group that have flown here from Paris half an hour ago. They are getting a Concord back late tonight. I apologize for the position I have put you in, but if you could summarize briefly and then, your entire statement will be placed in the record, in full.

Mr. ALVAREZ. Very well.

Another point I wish to make is that much has been said about the Japanese A-bomb survivor, however it is never subject to an independent review. There are a couple of questions being raised about the adequacy of this study in terms of serving as a basis for radiation risk estimates.

Recent findings by Lawrence Livermore Laboratory suggest that the neutron components of the atomic bombs may not have contributed as much to the total dose received as previously thought. This means that the observed cancer effect from the bombs may have been initiated at exposures a factor of two to three lower than previously believed. The DOE is reviewing the exposure data; it is not in the agency's long-term interest to admit that radiation exposures at low doses may be seriously underestimated.

Other human exposure to low levels of radiation data show greater cancer risks than the risks extrapolated by the ABCC/RERF data. Two principal data sets that contradict the A-bomb survivor study findings are the Oxford Survey by Dr. Alice Stewart and George Kneale, and the Hanford Survey by Dr. Mancuso.

The Oxford Survey is considered the largest epidemiological study in the world. With a sample of more than 15 million people, the Survey shows that fetal X-rays are linked to elevated risk of certain childhood cancers. The ABCC data shows that pregnant women, whose babies survived the carnage of the bombs, show lower cancer risks than other bomb survivors. This has led the DOE to conclude that Dr. Stewart's analysis must be wrong.

The Energy Department, however, has not addressed the question of whether the ABCC/RERF data constitutes a normal population, which the Oxford Survey is, for projecting risk estimates. I think there are some questions about the abnormality of the A-bomb survivors which deserves a further exploration.

Another issue is whether or not independent research by non-Government scientists can be continued after they assembled the data. This is the case of Dr. Mancuso. The University of Pittsburgh has been requesting data that Dr. Mancuso assembled on the Oak Ridge population to no avail. I think this is a situation unprecedented in the area of industrial epidemiology. Other industry studies under Government contract, such as berylium, asbestos and petrochemicals have permitted the investigators to keep the data they have day-to-day collected.

Were prisoners experimented upon with radiation for the benefit of NASA or the AEC? This question was raised by a 1963 AEC memorandum in which NASA employees expressed interest in exposing prisoners to ionizing radiation. Because the subcommittee did not fully pursue this, the record on this matter is ambiguous.

Between 1963 and 1973, the AEC irradiated the testicles of 131 men in Washington and Oregon State prisons. A newspaper article reporting the prisoner contract found that "primary benefits of the research will be for space exploration."

The prisoner experiment funds were approved by Drs. Burr, Barr, and Edington who all testified before the subcommittee in September. Dr. Edington, now Acting Assistant DOE Secretary for Health and the Environment, was a reviewer on this project who wrote in 1963:

> This proposal is a direct attack on our problem. I am for support at the requested level as long as we are not liable.

The third question deals with exploration of the LETBI/METBI program——

Mr. GORE. This is not on the point of epidemiology and if you could summarize it, I would appreciate it.

Mr. ALVAREZ. In looking through your hearing record, there were 57 records based on LETBI/METBI studies' 52 discussed thresholds of radiation damage and five addressing therapeutic efforts of the treatment to the patients. One of these papers, never published in a medical journal, states:

> It was not our plan to evaluate the long-range effectiveness of these relatively large individual doses of total body irradiation as a repetitive and sole therapy. This would have required establishing a sole treatment plan with this technique, which we were not prepared to do * * *. One should not infer from this study that we expected better clinical results than fractionated total-body or partial irradiation.

It is our opinion that the LETBI/METBI experiments deserve much more detailed review by respected scientists and experts in medical ethics. This review should also encompass all human studies conducted by and for the nuclear weapons and space industries over the past two decades.

I respectfully offer three recommendations for consideration.

One, to introduce legislation which would transfer all human health effects research on ionizing radiation from the DOE to HHS. It would read as follows:

> There are to be transferred to the Department of Health and Human Services all functions of the Department of Energy to research regarding the health effects of radiation on human beings, including those functions described in Sections 31 through 33 of the Atomic Energy Act of 1954, and Sections 103 and 107 of the Energy Reorganization Act of 1974, which related to research regarding the health effects of radiation on human beings.

This legislation will help prevent the abuses of the past from happening.

Other recommendations are: Two, to establish a congressionally mandated independent review of the Japanese atomic bomb survivor studies. This review should include recognized experts in the field who reflect a wide range of opinion.

Three, to allow the University of Pittsburgh to obtain copies of the Oak Ridge data so that an expanded analysis of the DOE work force can continue. The credibility of Federal radiation health effects research cannot be recovered as long as the nuclear weapons industry controls essential research in this area. It is for this reason that EPC strongly urges that the DOE be removed from the health effects research business altogether.

Thank you very much.

[The prepared statement of Mr. Alvarez follows:]

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STATEMENT
OF
ROBERT ALVAREZ
BEFORE
SUBCOMMITTEE ON OVERSIGHT AND INVESTIGATIONS
U.S. HOUSE OF REPRESENTATIVES
ON
FEDERAL RADIATION RESEARCH ACTIVITIES

May 19, 1982

Statement
of
Robert Alvarez
before
Subcommittee on Oversight and Investigations
U.S. House of Representatives
on
Federal Radiation Research Activities
May 19, 1982

Mr. Chairman and Members of the Subcommittee, I am Robert Alvarez, Washington Representative of the Environmental Policy Center (EPC), a non-profit environmental lobbying organization. I appreciate the opportunity to testify before the Oversight and Investigations Subcommittee on federal radiation health effects research activities. I commend Chairman Gore and the Members of the Subcommittee for their continuing interest in public and worker health protection. EPC has had an active interest in federal radiation research programs since 1975.

Perhaps it would be helpful to place the government's role in radiation research in historical context. This background information bears directly upon today's hearing.

BACKGROUND

Oversight hearings in 1977 by the Senate Commerce Committee and additional hearings in 1978 and 1979 by the House Commerce Health and Environment and Oversight and Investigations subcommittees initiated Congressional involvement in federal radiation health effects research. These investigations raised serious questions about the conduct of federal radiation research programs and resulted in passage of the Biomedical Research Extension Act of 1978 (P.L. 95-622). The act included a provision for the Department of Health and Human Services (DHHS) to coordinate radiation health effects research. An Interagency Radiation Research Committee (IRRC), chaired by HHS was formed with a Congressional mandate to provide Congress with a federal radiation research strategy by 1979.

In a parallel effort, President Carter formed an Interagency Task Force on Ionizing Radiation in 1978 to review federal radiation research and standard-setting activities. The task force recommendations agreed with Congress-- public health agencies should coordinate federal radiation research activities.

In 1981, the IRRC and National Academy of Sciences presented strategy documents to Congress. Both strategies, while similiar in major respects, have some differences which are now under study by the IRRC.

Currently, two IRRC subcommittees are working on recommendations for personnel requirements and uniform criteria for issuing and reviewing radiation research contracts to implement the federal radiation research strategy. The subcommittees are expected to report their recommendations to the Congress later this year. In addition, the National Cancer Institute is establishing a branch dedicated to low-level ionizing radiation health effects research.

This information about managing radiation research provides the context to examine the Department of Energy's (DOE) health effects research program at Oak Ridge Associated Universities and other institutions.

CONFLICTING INTERESTS

Despite these important steps, a central problem continues to erode public and scientific confidence in the ability of the government, especially DOE, to protect people from radiation--that is the continued dominance by the nuclear weapons bureacracy over radiation health effects research. In 1979, the President's Interagency Task Force on Ionizing Radiation determined that the DOE effectively controls over 60 percent of all federal radiation health effects research.[1] One merely has to read the Atomic Energy Acts of 1946 and 1954 and the Energy Reorganization Act of 1974 to ascertain that the Energy Department is in the business of making nuclear weapons and promoting nuclear energy. The DOE is not a public health agency.

This fundamental conflict-of-interest has created a record of suppression and distortion of science.[2] It has allowed the exposure of thousands of Americans to nuclear weapons radiation, which may now result in significant health damage and enormous financial liability for the Energy Department.

For example, the total damage claimed by residents living near the Nevada Test Site is estimated to be $2 billion.[3] The 1983 budget for DOE's nuclear weapons program is $5 billion.[4] An estimated 250,000 military personnel were involved in open air nuclear weapons detonations, many of these soldiers could have received dangerous exposures.[5] Swaths of land equaling hundreds of acres surrounding the Rocky Flat nuclear weapons plant near Denver, Colorado,[6] the Nevada Test Site,[7] and the Savannah River Plant[8] near Aiken, South Carolina are contaminated with plutonium released from DOE facilities. Preliminary evidence from health surveys of nuclear weapons workers,[9] radioluminizing workers,[10] atomic soldiers,[11] and downwind civilian residents[12] suggest increased human sensitivity to fatal cancer induction from levels of ionizing radiation considered "safe" by federal authorities.

As early as 1978, when many of these problems came to light through Congressional investigations, the Energy Department had already established a major "in-house" health effects research program influenced by the impact reductions in occupational exposure limits and compensation claims would have on DOE operations. These research programs fall into two catagories: epidemiological research of DOE and DOD contract employees and dose assessment from nuclear weapons testing.

Energy Department "sole source" contracts were let in 1978 to establish doses from fallout specifically to residents living near the Nevada Test Site. An advisory group was not formed until two years later. The Dose Assessment Advisory Group (DAAG), has since met regularly to review the work of these DOE contractors. The purpose of the Advisory Groups is to establish criteria for determining fallout doses. The criteria will be used in filing compensation claims in federal court and possibly other compensation avenues established by Congress. Contractors for the DAAG study are already testifying on behalf of the government in one of the court cases on fallout damage.[13] Testifying prior to completing the dose assessment placed the credibility of the dose assessment team in question.

The DOE epidemiology program deserves special attention because of the large number of DOE contract employees exposed to radiation who have reached the end of cancer latency periods. If Hanford, Oak Ridge and Savannah River worker populations were combined in one study it would rival the sample size of the Japanese Atomic Bomb Survivor studies, the current scientific basis for official risk estimates.[14] By the time Congress designated the HHS as the main coordinator of radiation health effects research, the DOE had already funded the most sensitive radiation epidemiology studies.

These studies include the nuclear naval shipyards and the Hanford, Oak Ridge, Savannah River, Los Alamos, Mound, National Lead, and Rocky Flats weapons facilities. The contracts for these studies were given out on a "sole source" basis without the standard competitive bidding, protocol submission, and peer review procedures inherent in federal public health agency research. Thus, the DOE has taken steps to prevent epidemiological research from developing outside its control.

For example, in 1974, the DOE decided to terminate funding for a health and mortality study of DOE contract employees directed by Dr. Thomas Mancuso of the University of Pittsburgh. Mancuso had refused to cooperate with DOE officials in downgrading a 1974 study of Hanford workers which suggested excessive cancer mortality among the Hanford workers.[15] He then later published positive findings on his own.[16] The DOE gave most of Mancuso's research project to Oak Ridge Associated Universities, with the exception of The Hanford study which went to Battelle - Northwest, a major nuclear contractor. The ORAU and Battelle contracts were let without proper protocol or peer review to groups with no significant background in epidemiology. In fact, ORAU received a contract even before it chose a principal investigator.[17]

Dr. Sidney Marks, who directs the Battelle study of the Hanford workers, was Dr. Mancuso's contract officer who orchestrated Mancuso's termination.[18] Dr. Ethyl Gilbert, who works under Dr. Marks, produced an analysis for the DOE in 1974 showing excessive cancer deaths among exposed Hanford workers.[19] DOE quickly buried the report. Drs. Marks and Gilbert have never referred to that analysis or explained in any of their written criticisms of the Mancuso study why they do not support its findings.

By 1980, ORAU was again without a principal investigator and was compelled by "in-house" DOE review to contract the Oak Ridge research out to the University of North Carolina. Again, this was done on a "sole source" contract basis without the standard review procedures. The University of North Carolina has a respected research program in the area of industrial medicine. ORAU, however, did not approach this department, and instead gave the contract to researchers with no significant experience in the field of industrial epidemiology.

These contract management practices are not conducted by public health research agencies such as the National Institutes of Health. This Fall, the Interagency Radiation Research Committee, chaired by the NIH, plans to issue recommended criteria for radiation health effects research contract review; these recommendations, we hope, will stop these abuses from occurring in the future. However, the problem of conflicting interests remains, relative to the most sensitive research areas influencing standard setting, compensation claims, and the future limits of nuclear weapons and nuclear power.

DOE'S HANDLING OF RESEARCH DATA

PAST RESEARCH AFFECTING CURRENT POLICIES: NEVADA TEST SITE AND FALLOUT

The blurred distinction between the DOE's bureaucratic self-interest and public health protection is well documented in several Congressional hearing records. Perhaps the most relevant Congressional findings to this Subcommittee's deliberations are contained in the House Commerce Oversight and Investigations Subcommittee report on the effects of nuclear weapons testing on people and sheep in southern Utah. The Commerce Subcommittee was particularly concerned about the Atomic Energy Commission's(AEC) handling of research used to deny claims filed by Utah sheepmen, whose flocks suffered inordinately high damage after a series of nuclear tests at the Nevada Test Site in 1953. The Subcommittee found:

1. "the government...inexcusably failed to give adequate warning to the sheepmen"
2. "knowingly disregarded and suppressed evidence correlating the deaths of sheep to radioactive fallout"
3. "exposure to radioactive fallout... was more likely than not, the cause of the 1953 deaths" and
4. "the government wrongly denied compensation to the sheep ranchers for losses."

The Department of HEW reached similar conclusions in its own investigation of this matter.

I bring this report, "The Forgotten Guinea Pigs,"to the Subcommittee's attention because the government research used to oppose the sheepmen's claims was conducted, in part, by Dr. Sidney Marks and Dr. Clarence C. Lushbaugh.

Dr. Marks coauthored a sheep study with Dr. Leo Bustad suggesting that radioiodine ingestion by the Utah sheep was too small to have caused significant injury.[20] Dr. Harold Knapp, in the 1978 Congressional hearings analyzed the Bustad/Marks study and found that "the material which appeared to have been withheld and distorted was the effects of radioiodine in the fallout ingested by pregnant ewes or fetal lambs."[21]

Dr. Lushbaugh, Chairman of ORAU's Medical Division, was commissioned by the AEC to study potential effects of fallout on the wool and skin of sheep. Lushbaugh in his study, "believed that although similarities were found to those (lesions) seen in the Cedar City (Utah) sheep, such lesions were found to be produced by physical and/or infectious agents." He concluded "that radiation was not the cause of death".[22] An AEC internal report of November, 1953, stating, "no positive evidence was found of an infectious organism that could account for the abnormal losses" of the Utah sheep did not change Lushbaugh's conclusions, which were used in court.[23] No consensus on the Lushbaugh findings was reached among AEC, state and U.S. Public Health officials. This situation prompted the AEC to fabricate a statement suggesting that all reviewers of the Lushbaugh study agreed with his conclusions. The Forgotten Guinea Pigs states... "By falsely using the October 27th statement, the AEC misrepresented the group's belief...and concluded that...the lesions were not produced by radioactive fallout."[24]

This Congressional investigation resulted in the sheepmen reopening their case against the government. Here we have past research of two DOE sponsored scientists, now in charge of highly sensitive research, criticized by a congressional report and by a federal public health agency, and subject to litigation involving fraud upon a federal court. Government credibility can only erode further with this kind of research management.

PAST RESEARCH EFFECTING CURRENT POLICIES: ATOMIC-BOMB SURVIVORS

The DOE, like its prececessor the AEC, controls the studies of Japanese atomic bomb survivors used to support current radiation risk estimates. This research is conducted under the auspices of the RERF with joint funding from the United States and the Japanese governments. Prior to the mid-1970s, the United States had total control over bomb survivor research through the ABCC. The ABCC data have never undergone independent scientific review.

There are major unanswered questions about ABCC reliability to justify low-level radiation standards for normal populations.

Recent findings by Lawrence Livermore Laboratory suggest that the neutron components of the atomic bombs may not have contributed as much to the total dose received as previously thought.[25] This means that the observed cancer effects from the bombs may have been initiated at exposures a factor of two to three lower than previously believed. The DOE is reviewing the exposure data; it is not in the agency's long-term interest to admit that radiation exposures at low doses may be seriously underestimated.

Other human exposure to low levels of radiation data show greater cancer risks than the risks extrapolated by the ABCC/RERF data. Two principal data sets that contradict the A-bomb survivor study findings are the Oxford Survey by Dr. Alice Stewart and George Kneale, and the Hanford Survey by Dr. Mancuso. The Oxford Survey is considered the largest epidemiological study in the world. With a sample of more than 15 million people, the Survey shows that fetal x-rays are linked to elevated risk of certain childhood cancers.[26] The ABCC data shows that pregnant women, whose babies survived the carnage of the bombs, show lower cancer risks than other bomb survivors.[27] This has led the DOE to conclude that Dr. Stewart's analysis must be wrong. The Energy Department, however, has not addressed the question of whether the ABCC/RERF data constitutes a normal population, which the Oxford Survey is, for projecting risk estimates.

RESEARCH EFFECTING CURRENT POLICIES: NUCLEAR WORKERS

Independent research on DOE workers is dampened by DOE's opposition to sharing data with Dr. Mancuso, who established positive findings among the Hanford workers and assembled the data. Despite repeated requests by the University of Pittsburgh, the Energy Department refuses to turn over the Oak Ridge data (reflecting the health and mortality experience of about 112,000 workers since 1943) to Dr. Mancuso. DOE contends that this data was collected under contract Union Carbide[28] when; in fact, the University of Pittsburgh held the contract to assemble and process that data at Oak Ridge under Dr. Mancuso's supervision.[29] This situation is unprecedented; in the asbestos, rubber, berylium, and chemical industries, where workers are also under study by government contractors, the data is the work product of the principal investigator.

The basic issue involved here is protection of principal investigators from government intrusion and data manipulation. It is an important area and does not have defined parameters. It is important for the University of Pittsburgh to obtain the Oak Ridge data so other academic institutions in the future are not subjected to government manipulation of research when bureaucratic interests are at stake.

The Hanford Survey examines data from 35,000 persons compared with the ATomic Bomb Casualty Commission/Radiation Effects Research Foundation data base of 110,000 persons. Mancuso's study suggests that chronic fractionated exposure to low-level radiation causes much different effects to emerge than single high doses. There was a marked increase in leukemia mortality among the A-bomb survivors[30] while in the Hanford Survey, excess multiple myeloma (bone marrow cancer) is found.[31] Dr. Alice Stewart, a respected radiation epidemiologist, has analyzed limited published data on the A-bomb survivors and suggests that about ten times more people died from the long-range effects of radiation exposure, particularly if non-cancers associated with bone marrow damage from high doses are factored in.[32]

Crucial scientific questions effecting low-level radiation standards and the baseline data used for government nuclear war scenarios must be answered. Subjecting the ABCC/RERF data to independent review and returning for the Oak Ridge data to Dr. Mancuso so the DOE employees study can be expanded will provide the needed answers.

HUMAN EXPERIMENTATION

Last fall, this Subcommittee explored allegations that a total body human irradiation project jointly funded by NASA and the AEC abused patients participating in the project. The Subcommittee is to be commended for its thorough investigation into this matter. The hearing record of this investigation raises even more serious questions than were addressed -- questions about the conflicting research agenda of the nuclear weapons industry:

1. Was this research program also receiving funds for nuclear weapons related research? On page 336 of the Subcommittee's hearing record, mention is made that the LETBI/METBI patients were part of a "mutually cooperative study" with the U.S. Army to determine "what levels of single, repeated, or protracted irradiation exposures result in the alteration of the bacteriologic

flora of persons exposed." This study was funded primarily by the Army but was also part of the AEC budget. At a symposium in 1967, dealing with post-attack scenarios after nuclear war, Dr. Lushbaugh presented data on a 12-year child exposed at LETBI.[33]

2. Were prisoners experimented upon with radiation for the benefit of NASA or the AEC? This question was raised by a 1963 AEC memorandum in which NASA employees expressed interest in exposing prisoners to ionizing radiation.[34] Because the Subcommittee did not fully pursue this, the record on this matter is ambiguous. Between 1963 and 1973, the AEC irradiated the testicles of 131 men in Washington and Oregon state prisons.[35] A newspaper article reporting the prisoner contract found that "primary benefits of the research will be for space exploration".[36]

This study was encouraged by scientists at Oak Ridge National Laboratories. For example, Dr. Eugene Oakberg, in support of the project in a March 12, 1963 letter to AEC official Paul Henshaw stated that: "It's too good a chance to miss, and well worth the money if we can put radiation response of the human testis on the same firm basis that we now have for experimental animals". Dr. Oakberg agreed to receive biopsy samples from the prisoners for analysis.

The prisoner experiment funds were approved by Drs. Burr, Barr, and Edington who all testified before the Subcommittee in September.[37] Dr. Edington, now acting Assistance DOE Secretary for Health and the Environment, was a reviewer on this project who wrote in 1963: "this proposal is a direct attack on our problem. I'm for support at the requested level as long as we are not liable."[38]

By 1965, Dr. Douglas Grahn, of Argonne National Labs, asked a principal investigator of the prisoner experiments to become a consultant for the NASA/NAS report on radiation exposure in space.[39]

The chairman of the Space Radiation Panel was Dr. Wright Langham of Los Alamos Scientific Laboratory. In 1945 and 1946 Dr. Langham participated in the injections of massive quantities of plutonium-239 into the veins of eighteen men, women, and children between the ages of 4 and 69 years.[40] He also participated in studies where normal "volunteers" were administered varying quantities of tritum, cesium-134, and cesium-137.[41] Dr. Langham was a reviewer of the LETBI/METBI program in the 1960s.

Finally, what does the publication record of the LETBI/METBI project suggest? We have identified 57 papers based on the LETBI/METBI studies fifty-two discussing thresholds of radiation damage and five addressing therapeutic effects of the treatment to the patients.[42] One of these papers, never published in a medical journal, states:

> It was not our plan to evaluate the long-range effectiveness of these relatively large individual doses of total body irradiation as a repetitive and sole therapy. This would have required establishing a sole treatment plan with this technique, which we were not prepared to do.... One should not infer from this study that we expected better clinical results than fractionated total-body or partial irradiation.[43]

The authors concluded that the end point of their treatments was to define the "range of clinical and hematologic effects that single expsoures of 50 to 100R can be expected to produce in these diseases". The authors reiterated that the study: "will not (1) demonstrate that 50 or 100R is better than currently accepted fractionation modes, or (2) analyze the long-range effectiveness of these doses." [44]

It is our opinion that the LETBI/METBI experiments deserve much more detailed review by respected scientists and experts in medical ethics. This review should also encompass all human studies conducted by and for the nuclear weapons and space industries over the past two decades.

RECOMMENDATIONS

I respectfully offer three recommendations for consideration.

1. To introduce legislation which would transfer all human health effects research on ionizing radiation from the DOE to HHS. It would read as follows:

> There are to be transfered to the Department of Health and Human Services all functions of the Department of Energy to research regarding the health effects of radiation on human beings, including those functions described in Sections 31 through 33 of the Atomic Energy Act of 1954 and Sections 103 and 107 of the Energy Reorganization Act of 1974 , which related to research regarding the health effects of radiation on human beings.

This legislation will help prevent the abuses of the past from happening again.

Other recommendations are:

2. To establish a congressionally-mandated independent review of the Japanese Atomic Bomb survivor studies. This review should include recognized experts in the field who reflect a wide range of opinion;

3. To allow the University of Pittsburgh to obtain copies of the Oak Ridge data so that an expanded analysis of the DOE workforce can continue. The credibility of federal radiation health effects research cannot be recovered as long as the nuclear weapons industry controls essential research in this area. It is for this reason that EPC strongly urges that the DOE be removed from the health effects research business altogether.

This concludes my statement. Thank you.

Footnotes

1. Interagency Task Force on the Health Effects of Ionizing Radiation, Report of the Work Group on Science, U.S. Department of Health, Education and Welfare 1979, p. 28.

2. U.S. Congress, House Committee on Interstate and Foreign Commerce, Subcommittee on Health and the Environment, Effect of Radiation on Human Health, 95th Cong. 2nd Sess., Serial Nos. 95-179, 95-180, Vols. I and II, January 24-26, February 8,9, 14 and 28, July 11, 12, 13, and 14 , 1978.

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4. Department of Energy National Security Programs Authorization Act of 1981.

5. Statement of Donald M. Kerr, Acting Assistant Secretary for Defense Programs, Department of Energy, Effect of Radiation on Human Health, January 26, 1978, pp.331-404.

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Johnson, C.J., " Cancer Incidence in an Area Contaminated with Radionuclides Near a Nuclear Installation", Ambio, Vol X, No. 4, 1981, pp 176-81.
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13. Dr. Lynn Anspaugh, OREP Scientific Director, Lawrence/Livermore National Laboratory and a contractor belonging to the Dose Assessment Task Group, presented data on uptake of radionuclides by sheep on behalf of the government on May 14, 1982 before the Federal District Court in Salt Lake City Utah, concerning Bulloch v. the USA.

14. The debate over the question of sample size and low-dose human studies focuses on two issues: (a) assumptions that the current risk estimates based on extrapolations from high dose studies are correct. For example, if the BEIR III(1980) estimates are applied , for every million people exposed to one rem of radiation there would be about 77 to 226 radiation induced cancer deaths. If, the estimates derived from low-dose studies are used there would be as many as 7000 radiation induced cancer deaths. In the absence of empirical evidence, the supporters of the high dose studies, must rely on animal, cellular expiriments and extrapolations. However, low-dose human studies (see refs. 8-12) suggest higher risk coefficients. (b) assumptions that the effects of low-level radiation are so small that prohibitively large sample sizes are required to observe true effects. The principal proponent of this view is Dr. Charles Land of the National Cancer Institute and is contained in a Science article (Sep. 80). Dr. George Kneale, a statistician with the University of Birmingham, England in a paper delivered to the Nuclear Regulatory Commission on Nov. 1980 points put that Land's theory is based on a mathematical model which assumes that all cells are homogenous. This is of course not the case. There are cells which are more sensitive to radiation damage than others (ie red marrow).

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18. In a draft memorandum from Sidney Marks, dated Feb. 20, 1973, Marks states, "unless an immediate replacement /_for Mancuso/ is found, a public charge may be made that thr AEC is stopping the the program out of fear that positive findings will emerge." Marks continued by adding,"... overtures to possible candidates must be carried out in a clandestine atmosphere..." to replace Mancuso.

Later, according to Dr. Theofore Sterling (see Ref. 17)"moves were made

18. (cont.) instituted to remove Mancuso from the study, or rather to remove the study from Mancuso. Administrative reasons cited for the action were later examined by the Subcommittee on Health and the Environment. In summary, the reasons for removing Mancuso were that :(a) he was about to retire;(b) he failed to publish his findings:(c)his scientific peers recommended limiting, terminating or selecting another investigator in his place.

"However, Congressional hearings brought out quite an opposite set of facts. Dr. Mancuso was not about to retire. An internal memorandum of the Department of Energy actually praised Mancuso for not'prematurely' publishing earlier positive finding of increased cancer rates among the Hanford employees.Moreover, a peer review committee had actually recommended continuation rather than termination of Mancuso's contract."

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The authors concluded, "we have established that there is a relationship between cancer as a cause of death and the total external dose recieved".

AEC Hanford Research Director, Alex Fremling in draft memoranda to central AEC management found that"the Battelle data suggest that Hanford has a higher proportion of cancer deaths for those under 65 than the United States as a whole or that of the state of Washington as a whole." Fremling continued"the analysis tends to show a much higher incidence of certain types of cancers among those who have had 6R and above throught their lifetime." The AEC official concluded" we hoped to get a good answer to the Milham report, and instead it looks like we have support for it."

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44. Ibid.

Mr. Gore. Thank you. And again I apologize for putting you——

Mr. Alvarez. I would also like to put in the record, if I may, a paper that will appear in the British Journal of Epidemiology on the A-bomb survivor study.

Mr. Gore. We will look at that later and make a decision on that.

Without objection, the record will be held open for questions that we would like to submit to you and also I would like to hold the record open in fairness for those who object to some of the statements you have made so they can respond to them, if they wish to do so.

[The paper mentioned above follows:]

DELAYED EFFECTS OF A-BOMB RADIATION

A review of recent mortality rates and risk estimates for 5 year survivors

by

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ABSTRACT

A review of published data relating to A-bomb survivors has led to the conclusion that, since they were based on the mortality experiences of 5 year survivors, estimates of radiation effects should have been controlled for two opposing forces, namely, selective survival of exceptionally fit persons during the period of heavy acute mortality and residual disabilities. Both effects were dose-related and beyond question, and the disabilities probably included the effects of incomplete repair of bone marrow damage. Therefore, in addition to differences between high and low dose being largely obliterated, there was probably distortion of cancer effects. The two opposing forces are clearly the reason why the change from the high mortality rates of 1945-46 to the low rates of the 1950s was not accompanied by a change from a positive to a negative association with dose, and imperviousness to the residual disabilities is probably the reason why sudden deaths of previously healthy persons (exemplified by suicides) were an exception to this rule. Finally, impairment of bone marrow function probably accounts for the early epidemic of myeloid leukaemia; the apparent absence of other cancers at this time, and the relatively high, dose-related death rates for blood diseases other than leukaemia.

INTRODUCTION

More and more the question of how best to obtain estimates for cancer and other mutational effects of ionizing radiation is engaging public attention.(1,2) This upsurge of interest in a subject of obvious importance to modern society has coincided with some disturbing findings: after a long period of assuming that estimates for A-bomb survivors - which were internally consistent and in close agreement with other observations - were of direct relevance to radiation workers and the general public,(3) a survey of workers in the nuclear industry has produced estimates which are an order of magnitude higher than the earlier ones and have different implications for solid tumours and leukaemias.(4,5,6) There have been numerous attempts to discredit the worker-based estimates(7,8,9,10) but this time it is the survivor-based estimates which are under fire.(11,12)

The source of these estimates is a Life Span Study (LSS) population of approximately 80,000 persons, identified through census records 5 years after the bombing of Hiroshima and Nagasaki. To be more precise: the two cities were bombed in August 1945; the follow-up began in October 1950 and, for purposes of estimating radiation effects, the study population was eventually restricted to 79,736 persons with estimated (T65) doses. In this population there was better representation of persons who were within range of potentially lethal doses of radiation (approximately 100%) than of persons from more distant locations (approximately 30%). .Therefore the mean radiation dose (24 rads) is higher than the estimate for all 5 year survivors (approximately 285,000 persons with an estimated mean dose of 17 rads). Even so there were 34,634 persons with near zero doses and a further 20,502 with estimated doses of less than 10 rads (Table 1).

From time to time these dose-level subgroups have been compared with national statistics (standardised mortality ratio or SMR analysis)(13,14,15) but all estimates of radiation effects are based on internal comparisons similar to the ones in Table 1 and now available for 6 calendar year periods (relative risk analysis with control for sex, exposure age and city). On these terms the only causes of death which have ever shown any evidence of radiation effects are (i) leukaemia, with special emphasis on early years (1950-58) and the more acute forms of myeloid leukaemia; (ii) other blood diseases, whose involvement could be an artifact due to difficulty in distinguishing between aplastic anaemia and leukaemia, and (iii) solid tumours, now the cause of more radiogenic deaths than leukaemia but with much weaker involvement than myeloid leukaemia and little in the way of dose-related mortality rates before 1960.

The mortality rate for diseases other than cancer has never shown any signs of being either elevated or dose-related.(11,14) Therefore in a series of mortality reports, originally sponsored by the Atomic Bomb Casualty Commission (ABCC) and now the responsibility of the Radiation Effects Research Foundation (RERF) (and culminating in the relative risk analysis of 1950-74 deaths(11)), there have been many reiterations of the following claims. The first conclusion is that there has been no involvement of 5 year survivors in non-cancer effects of the radiation and therefore a normal risk of dying from natural causes (including cancers) at all dose levels since October 1950. The second conclusion is that the much earlier involvement of leukaemia than solid tumours is purely the result of latent period differences, and the much greater involvement of myeloid leukaemia than other neoplasms is because bone marrow is more sensitive to cancer induction by radiation than other tissues. Hence a general conclusion, namely, that we can expect early warning of any cancer hazard for radiation workers, and that this will take the form of extra deaths from myeloid leukaemia.

This interpretation of the mortality experiences of A-bomb survivors has held sway for many years and is still the basis of all safety recommendations approved by the International Commission on Radiation Protection (ICRP).(16) It is, however, dependent upon the findings for blood disease being an artifact and, more importantly, upon a survivor population, which began by being strongly biased in favour of exceptionally healthy persons, losing this advantage in less than 5 years.

EARLY EFFECTS OF THE BOMBING

Death from hitherto unknown syndromes, all caused by extensive destruction of bone marrow and other internal organs by the radiation and heralded by the now classic "radiation sickness" symptoms, was the fate of many persons who had either survived more immediate effects of the bombing (e.g. blast injuries and radiation burns) or had no evidence of radiation effects apart from the sickness.(17) Therefore, over and above the usual reasons why all survivor populations are necessarily biased in favour of exceptionally healthy persons (survival of the fittest or healthy survivor effect), there was a brand new reason exerting direct effects on general haemopoesis and the immune system.

Both the usual and the exceptional component of the healthy survivor effect were strongly dose-related. Therefore the question we should be asking ourselves is why the change from the fantastically high death rate of the first 6 months to the near normal rate of the 1950s was not accompanied by a change from a positive to a negative association with dose (Table 1). The high dose levels of the LSS population (assembled in October 1950) were the most strongly biased in favour of persons who were highly resistant to diseases and injuries in August 1945. Therefore, in the normal course of events, we would have expected them to have much the lowest death rates. This very reasonable expectation was, in fact, fulfilled for one cause of death, namely, suicide. Therefore there is a subsidiary as well as a main problem, namely, why deaths from self-inflicted injuries differed from other accidental deaths.

Though early deaths of first day survivors were numbered in thousands, there were many persons who eventually recovered from their injuries or illnesses with or without obvious residual disabilities.(17) Therefore it is inconceivable that no member of the LSS population had any residual disabilities and possible that the less obvious ones included incomplete repair of bone marrow damage and consequent effects on infection sensitivity and blood diseases.

NET EFFECT OF TWO OPPOSING FORCES

According to this hypothesis some cancellation of the healthy survivor effect by residual disabilities is an inevitable consequence of all natural and man-made disasters. In the case of Hiroshima and Nagasaki the addition of marrow damage to more obvious disabilities both prevented full expression of mutational effects of the radiation (either cancers or inherited defects) and left the non-cancer death rate reflecting almost equal pressures by two opposing forces, namely, selection in favour of exceptionally fit persons and incomplete healing of blast injuries and tissue destructive effects of the radiation.

On these terms all dose-level comparisons would require some control of the healthy survivor effect and, without this, one would be left with (false) impression of no mutational effects at low dose levels. Furthermore, given near equality of the two opposing forces, it would be easy to overlook certain possibilities. For example, the temporary absence of a dose-related death rate for solid tumours could be due to extra, radiogenic cases (whose latency periods had been shortened by the bone marrow damage), falling into gaps created by shortages of normal cancers or cases initiated before August 1945 which therefore became merged with all the other causes of extra death during the period of heavy acute mortality. Likewise, the early epidemic of myeloid leukaemia could be a direct consequence of bone marrow damage and therefore something which would not be expected to follow exposure to worker doses or background radiation.

RESIDUAL BONE MARROW DAMAGE

Evidence for or against there being residual bone marrow damage would require careful testing of specific hypotheses. Therefore there is little of value to be found in reports which have never envisaged this possibility. However, Beebe, Kato & Land, after completing their relative risk analysis of 1950-74 deaths. did proceed to test a new hypothesis which had grown out of experimental work. The hypothesis was that exposure to ionizing radiation accelerates the natural ageing process,(15) and the test by Beebe *et al* was prefaced with the following statement: "In this report we examine the mortality experience of the A-bomb survivors more closely than has been done before, using recent tabulated information on deaths through September 1974, and explore the question of bias from the heavy acute mortality".

In practice evidence of the postulated effect of the radiation was sought in a series of dose-level comparisons (with national statistics setting the standards of normality) after exclusion, first, of all deaths from neoplasms and injuries, and, later, of deaths from blood diseases other than leukaemia. The later exclusions were made after division of diseases other than neoplasms into 6 diagnostic groups had produced 5 sets of what were deemed to be negative findings in a mortality analysis which recognised 2 groups of survivors (Hiroshima and Nagasaki) and 5 dose levels (Table 2). For the group as a whole there was unmistakable evidence of a rising trend of mortality in Hiroshima but not Nagasaki, also evidence of exceptionally low SMRs in the oldest age group (over 50 years in 1945).

Finally, in their discussion of these findings and other reports, Beebe et al admit that with mortality "falling rapidly with increasing distance from the hypocentre, selection is an indubitable fact not an issue". However, they made no attempt to control for this factor and ignored a second axiom, namely, that following extensive injuries some permanent crippling is a fact not an issue. In short, as a way of testing the only new hypothesis for many years, Beebe and his associates have used their original method without control for any new factor and without even a passing thought for their own exceptional findings for suicide (Table 1).

In a survivor population sudden accidental death would have less chance of being influenced by residual disabilities than other modes of dying and, if residual disabilities included bone marrow damage, there could be a substantial difference between sudden deaths due to violence and later deaths from less overwhelming injuries. Therefore it is unfortunate that the decision not to include injuries in the test of the new hypothesis has left us without any SMRs for deaths from self-inflicted injuries. Nevertheless, there is much of interest to be found in Table 2.

Thus for the 5 large groups of non-cancer deaths the rates were consistently lower for Hiroshima survivors, who included less than 10% of persons whose doses were high enough to cause tissue damage (over 100 rads), than Nagasaki survivors with more than 20% of such persons. Furthermore, in both cities, the group of non-cancers with the highest proportion of sudden deaths (cerebrovascular accidents) had exceptionally low SMRs; the group most directly concerned with general haemopoesis (blood diseases) had much the highest ratios, and the only identifiable infection (tuberculosis) had ratios which were well above average also much higher for Nagasaki than Hiroshima survivors.

CITY DIFFERENCES

The fact that Hiroshima survivors have always had lower death rates than Nagasaki survivors is supposed to be the result of unidentified socio-economic factors.(13) However, the differences in Table 2 are suggestive of stronger opposition to the healthy worker effect by residual disabilities in Nagasaki than Hiroshima. In favour of this hypothesis are, first, the higher dose levels and, secondly, although there were more sudden deaths after the first than the second bomb, the August to December death rate for first day survivors was much higher in Nagasaki than Hiroshima (Table 3). Therefore, from the point of view of delayed effects of the radiation it is probably of more importance that the first bomb exploded over a delta and the second bomb over a narrow valley surrounded by hills, than that the two bombs were not exactly alike.(18)

BLOOD DISEASES

The group of blood diseases, with aplastic anaemia as the main component, is the only diagnostic group in Table 2 with an elevated and dose-related death rate. This has always been so(11) yet we are asked to believe that all exceptional findings for blood diseases other than leukaemia are the result of misdiagnoses.(15) In support of this hypothesis is the fact that a review of 59 cases by the Leukaemia Registry in Hiroshima led to 13 cases being reclassified as leukaemia (9) or other cancers (4). The rejected cases had relatively high doses. Nevertheless their exclusion still left more observed than expected deaths and the same dose-level ranking of SMRs (Table 4). Table 4 also shows that applying similar "corrections" to the remaining 58 cases still left evidence of a dose-related effect.

These findings make it impossible to agree with Beebe et al that "a superficial association between mortality from diseases of blood and blood forming organs and radiation rests entirely upon the carcinogenic effects of radiation, mainly the leukaemogenic effect." This statement, like so many conclusions of ABCC reports, is indicative of an obsession with possible mutational effects of ionizing radiation to the exclusion of all else. Yet it was widely known that the threshold dose for bone marrow damage was relatively low and that aplastic anaemia is the most easily recognised effect of such damage.

ESTIMATES OF RADIATION EFFECTS

If the mortality experiences of A-bomb survivors are being influenced by a survivor effect and residual disabilities, neither comparisons with national statistics or with a zero dose level will provide the correct standard for estimating radiation effects. What is needed is a cause of death which (i) is not affected by one or other of the opposing forces, and (ii) can be compared with national statistics. The first requirement rules out everything except sudden deaths of previously healthy persons, and the second rules out sudden deaths but leaves deaths from cerebrovascular accidents as a possible alternative. Unlike suicides these deaths have never shown any signs of a negative correlation with dose but for many years the rate for Hiroshima survivors was about 30% below the national rate. Therefore it is reasonable to assume that as a result of the heavy acute mortality, the risk of dying from natural causes was at least 30% below par for all 5 year survivors ("correction factor" for the healthy survivor effect).

Since cancers and injuries were not included in the SMR analysis of 1950-74 deaths it is only possible to produce estimates of extra, radiogenic deaths for the period 5 to 22 years after the bombing (see 7th Mortality Report with observed and expected deaths for 1950-72).(13) During these years there were 18,526 deaths from all causes and 3,744 cancer deaths. By national standards the corresponding expectations were 20,182 and 3,283. Therefore, after correction for the healthy surviver effect, the ratio of observed to expected deaths was 3,744 ÷ 2,298 or 1.62 for cancers and 14,748 ÷ 11,829 or 1.25 for non-cancers. On these terms 1,446 or 39% of the 1950-72 cancer deaths were radiation-induced. For other deaths the corresponding estimates are 2,953 or 20%, and for all deaths they are 4,399 or 24%.

Included in the relative risk analysis of 1950-74 deaths are estimates of extra radiation deaths for all 5 year survivors (approximately 285,000 persons, see Table 3). As usual they are based on dose level comparisons within the LSS population and they assume linearity of dose response. On these terms the only extra deaths were either leukaemias (192 cases) or solid tumours (223 cases) and accompanying these 415 radiogenic deaths there were approximately 70,000 deaths from natural causes. Therefore, even on the unlikely assumption that (i) there was no involvement of deaths from cerebrovascular accidents in residual disabilities; (ii) there were no radiation-induced deaths after 1972, and (iii) all extra deaths were contained within the LSS population, the revised estimates for extra radiogenic deaths are over 10 times higher than the ones currently approved by ICRP.(16)

DISCUSSION

According to the "silent forces" hypothesis, the fact that the LSS population of A-bomb survivors has always recorded relatively low rates of general mortality is a direct consequence of the exceptionally high rates during the immediate aftermath of the explosions. During this period of devastation the risk of dying either from natural causes or special effects of the A-bomb must have been exceptionally high for anyone who, for whatever reason, was already in a poor state of health or nutrition. Therefore, among persons who were eligible for inclusion in the study population of 5 year survivors there must have been too few naturally weak persons and too many naturally strong (i.e. exceptionally healthy) persons and a general bias in favour of well to do families.

This effect of the bombing is admitted by Beebe, Kato & Land(15) but neither they nor the authors of earlier reports have been prepared to admit that, given this inevitable bias, their findings can no longer be accepted at face value.

The present review has found even the firmest of earlier conclusions unacceptable, not only for conjectural reasons but also because the findings for blood diseases other than leukaemia are not adequately explained in terms of misdiagnosis and therefore require delayed effects of the radiation to include tissue damage as well as mutations. Furthermore, since the principal target of all radiation effects (immediate or delayed) is bone marrow, there was, over and above the usual reasons for expecting a (dose-related) healthy survivor effect, a special factor - with direct effects on the immune system and general haemopoesis - which was contributing both to the healthy survivor effect and to residual disabilities.

This brings us to the nub of the problem: can the straightforward analyses of dose-related death rates - which are the basis of current beliefs about the health risks of radiation workers - be regarded as robust under the conditions which undoubtedly existed. On reflection it is easy to see that they are not. For example, the idea that an increased prevalence of myeloid leukaemia will necessarily be the first sign of any ill effects from radiation-induced mutations makes no allowance for the possibility that, in the case of A-bomb survivors, bone marrow damage both aided rapid development of post-bomb cancer inductions and added to an already high risk of latency deaths for earlier inductions. Therefore, the fact that the 1950-58 mortality rates for most forms of cancer were not dose-related is important since this is exactly the finding one would expect if most of the extra, radiogenic cases were filling gaps caused by pre-1950 (latency) deaths of non-radiogenic cancers. In favour of this interpretation of the data is evidence from a survey of childhood cancers which suggests that immune system defects are early concomittants of the cancer process and have often been the cause of latency deaths ascribed to respiratory infections.(19)

In the Hanford study the risk of dying from natural causes was found to be much lower for the workers than for the nation as a whole, also lower for workers in high than low risk occupations.(6,9) However, unlike the healthy survivor effect, whose dose-related consequences were caused by the radiation, the healthy worker effect (also dose-related) predated all exposures and was clearly the result of deliberate recruitment of exceptionally healthy persons into the more dangerous jobs.(6) A healthy worker effect is common to many industries.(20) Therefore detection of mutational effects of radiation should be much easier in a worker than a survivor population. This has proved to be so and the nature of the most distinctive effect of the worker doses (multiple myeloma) suggests that we are right to assume that bone marrow is exceptionally sensitive to cancer induction by radiation but wrong to assume that without bone marrow damage the resulting cancers will be myeloid leukaemias.

Thus far only a small fraction of the data relating to workers in the nuclear industry has been examined for evidence of radiation effects, and none has yet been examined for evidence of second or third generation effects. However, there is no shortage of radiation worker dose records and where they are most plentiful (i.e. in the United States) there are also unusually good opportunities for relating the data both to death certificates of ex-workers (via Social Security claims) and to medical records of mentally or physically defective offspring of workers (via the same system). Therefore research workers should be dissuaded from taking the short cut advocated by Land(2) (since this requires extrapolation of high dose observations to low dose levels) and encouraged to make full use of data already collected during the course of a special study (i.e. a study of the lifetime health and mortality experiences of employees of AEC Contractors)(21) which was incidentally the source of Hanford data.

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TABLE 1

Relative Risk Analysis of 1950-74 Deaths for the purpose of detecting Radiation Effects : From Beebe, Kato & Land 1977(6)*

Dose Levels in rads	Relative Risk(1)							All Deaths (1950-74)	Persons at Risk(1950)	Death Rate
	All Causes	All Neoplasms	Leukaemia	All Injuries	Suicide	Other Diseases	Blood Diseases			
0	1.00	1.00	1.00	1.00	1.00	1.00	1.00	8607	34343	23.3
1-9	1.00	1.01				1.00		4933	20502	24.1
10-49	0.99	1.06	1.41	0.87	0.64	0.98	1.35	3635	14520	25.0
50-99	0.98	1.07	1.77	1.00	0.98	0.96	1.43	1025	4032	25.5
100-199	1.08	1.25	5.22	0.94	0.81	0.96	2.61	740	3112	23.8
200-299	1.06	1.72	10.80	0.55	0.12	0.94	4.08	317	1404	22.6
300-399	1.01	1.48	18.90	0.62	0.00	0.91	4.59	138	640	21.6
400 +	1.32	2.12	23.13	1.33	0.40	1.10	6.96	248	883	28.1
Deaths No. %	19646 100.0	4031 20.5	144 0.7	1210 6.2	395 2.0	14405 73.3	117 0.6	19646	79736	24.6
Test(2) Statistic	0.000*	0.000*	0.000*	0.720	0.999+	0.610	0.000*	-	-	

(1) With control for sex, exposure age and city

(2) Test of increasing linear trend - *significant increase in risk with rising dose
+significant decrease in risk with rising dose

TABLE 2

SMR Analysis of 1950-74 Deaths for the purpose of testing the Hypothesis of Radiation Accelerated Ageing
From Beebe, Kato & Land 1978(14)

City	Dose level in rads.	Standardised Mortality Ratios							Persons At Risk	
		Tuberculosis	Cerebro-vascular	Other Cardio-vascular	Digestive	Blood	Residue	Total excl. Blood	Nos.	%
Hiroshima	0	94	76	89	98	134	88	84	29943	49.5
	1-9	111	75	89	88	153	87	83	13796	22.8
	10-49	122	72	84	97	226	78	80	10761	17.8
	50-99	99	79	105	94	240	79	85	2718	4.5
	100+	97	80	92	113	460	91	88	3252	9.8
	Total	103	75	89	94	178	86	83	60470	100.0
Nagasaki	0	150	93	105	104	148	123	107	4700	24.4
	1-9	171	98	102	122	101	112	108	6706	34.8
	10-49	188	98	115	102	35	103	107	3759	19.5
	50-99	106	84	130	102	102	85	95	1314	6.8
	100+	146	90	110	108	550	109	104	2787	21.3
	Total	160	95	110	105	162	110	106	19266	100.0
No. of Deaths	Hiroshima	753	3355	2261	1238	94	3524	11131	11225	77.9
	Nagasaki	336	925	604	328	23	964	3157	3180	22.1
Total No.		1089	4280	2865	1566	117	4488	14288	14405	100.0
%		7.5	29.7	19.9	10.9	0.8	31.2	99.2	100.0	

TABLE 3

Early Effects of the Bombing
Differences between the two Cities[1]

Early Effects of the Bombing		Hiroshima		Nagasaki	
		No.	%	No.	%
First Day	Fatal Injuries	45,000	17.6	22,000	12.7
	Other Injuries	91,000	35.7	42,000	24.1
	Not Injured	119,000	46.7	110,000	63.2
	Total	255,000	100.0	174,000	100.0
Next 4 months	Fatal Injuries	19,000	20.9	17,000	40.5
	Other Injuries	72,000	79.1	25,000	59.5
	Total	91,000	100.0	42,000	100.0
1950 Census Population of survivors		285,000			

(1) From Ohkita, 1975(17)

TABLE 4

SMR Analysis of Blood Disease Deaths : Effect of removing Suspect Cases(1)

Diseases of blood and blood forming organs	Dose level in rads.	Original Notifications			Revised Diagnosis		
		Observed	Expected	SMR	Observed	Expected	SMR
Leukemia Registry Cases	0-9	30	22.9	131	29	22.9	127
	10-99	15	7.3	205	12	7.3	164
	100+	14	2.3	609	5	2.3	217
	Total	59	32.5	182	46	32.5	142
Other Cases	0-9	33	22.6	146	32	22.6	142
	10-99	15	7.1	211	12	7.1	169
	100+	10	2.3	435	4	2.3	174
	Total	58	32.0	181	48	32.0	150

(1) From 8th Mortality Report(11) see also Beebe, Kato & Land(15)

Mr. **Gore**. Again I apologize to you and all of the witnesses today for the untenable position that we have put you in.

And now I am going to go down and make some more explanations downstairs.

The hearing is adjourned.

[Whereupon, at 6:35 p.m., the subcommittee was adjourned.]

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